# Freeform Search

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| DB Name | Query | Hit Count | Set Name |
|---|---|---|---|
| USPT,JPAB,EPAB,DWPI | bessis-a$.in. | 3 | L13 |
| USPT,JPAB,EPAB,DWPI | picciotto-m$.in. | 3 | L12 |
| USPT,JPAB,EPAB,DWPI | changeux-j$.in. | 4 | L11 |
| USPT,JPAB,EPAB,DWPI | l9 and promoter | 16 | L10 |
| USPT,JPAB,EPAB,DWPI | l3 and l5 | 17 | L9 |
| USPT,JPAB,EPAB,DWPI | l7 and promoter | 10 | L8 |
| USPT,JPAB,EPAB,DWPI | l2 and l5 | 11 | L7 |
| USPT,JPAB,EPAB,DWPI | l1 and l5 | 0 | L6 |
| USPT,JPAB,EPAB,DWPI | neuronal adj1 nicotinic adj1 acetylcholine adj1 receptor$1 | 101 | L5 |
| USPT,JPAB,EPAB,DWPI | l1 or l2 or l3 | 9680 | L4 |
| USPT,JPAB,EPAB,DWPI | ((536/23.1 \|536/23.5 \|536/23.51 \|536/24.1 )!.CCLS. ) | 7704 | L3 |
| USPT,JPAB,EPAB,DWPI | ((435/455 \|435/467 \|435/325 \|435/368 )!.CCLS. ) | 3527 | L2 |
| USPT,JPAB,EPAB,DWPI | ((800/8 \|800/9 \|800/10 \|800/13 \|800/18 \|800/21 \|800/22 \|800/25 )!.CCLS. ) | 324 | L1 |

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 ********** STN Columbus **********
**

FILE 'HOME' ENTERED AT 09:24:45 ON 21 SEP 2000

=> file medline

COST IN U.S. DOLLARS                SINCE FILE     TOTAL
                                    ENTRY  SESSION
FULL ESTIMATED COST                    0.15     0.15

FILE 'MEDLINE' ENTERED AT 09:24:53 ON 21 SEP 2000

 FILE LAST UPDATED: 15 SEP 2000 (20000915/UP). FILE
COVERS 1960 TO DATE.

 MEDLINE has been reloaded to reflect the annual MeSH changes
made by
 the National Library of Medicine for 2000. Enter HELP RLOAD for
details.

 The OLDMEDLINE file segment now contains data from 1958
through 1965.
 Enter HELP CONTENT for details.

 Left, right, and simultaneous left and right truncation are available in
the
 Basic Index. See HELP SFIELDS for details.

 THIS FILE CONTAINS CAS REGISTRY NUMBERS FOR EASY
AND ACCURATE
 SUBSTANCE IDENTIFICATION.

=> s neuronal/ab,bi

      80711 NEURONAL/BI
    5413360 AB/FA
      66007 NEURONAL/AB
            (NEURONAL/BI (L) AB/FA)
      80711 NEURONAL/BI
L1    80711 NEURONAL/AB,BI

=> s l1 and (transfect? or transform? or transduc?)/ab,bi

      70593 TRANSFECT?/BI
    5413360 AB/FA
      45486 TRANSFECT?/AB
            (TRANSFECT?/BI (L) AB/FA)
      70593 TRANSFECT?/BI
     214836 TRANSFORM?/BI
    5413360 AB/FA
     107557 TRANSFORM?/AB
            (TRANSFORM?/BI (L) AB/FA)
     214836 TRANSFORM?/BI
      91974 TRANSDUC?/BI
    5413360 AB/FA
      49924 TRANSDUC?/AB
            (TRANSDUC?/BI (L) AB/FA)
      91974 TRANSDUC?/BI
L2     5827 L1 AND (TRANSFECT? OR TRANSFORM? OR
TRANSDUC?)/AB,BI

=> s l2 and toxin#/ab,bi

      58774 TOXIN#/BI
    5413360 AB/FA
      39784 TOXIN#/AB
            (TOXIN#/BI (L) AB/FA)
      58774 TOXIN#/BI
L3      180 L2 AND TOXIN#/AB,BI

=> s l3 and vivo/ab,bi

     267353 VIVO/BI
    5413360 AB/FA
     230827 VIVO/AB
            (VIVO/BI (L) AB/FA)
     267353 VIVO/BI
L4      18 L3 AND VIVO/AB,BI

=> d 1- bib ab

YOU HAVE REQUESTED DATA FROM 18 ANSWERS -
CONTINUE? Y/(N):y


L4  ANSWER 1 OF 18  MEDLINE
AN  1999343779    MEDLINE
DN  99343779
TI  Chemokine receptor expression and signaling in macaque and
human fetal
    neurons and astrocytes: implications for the neuropathogenesis of
AIDS.
AU  Klein R S; Williams K C; Alvarez-Hernandez X; Westmoreland
S; Force T;
    Lackner A A; Luster A D
CS  AIDS Research Center, Massachusetts General Hospital, Harvard
Medical
    School, Charlestown 02129, USA.. klein.robyn@mgh.harvard.edu
NC  AI01519 (NIAID)
    CA69212 (NCI)
    AI40618 (NIAID)
    +
SO  JOURNAL OF IMMUNOLOGY, (1999 Aug 1) 163 (3) 1636-46.

    Journal code: IFB. ISSN: 0022-1767.
CY  United States
DT  Journal; Article; (JOURNAL ARTICLE)
LA  English
FS  Abridged Index Medicus Journals; Priority Journals; Cancer
Journals
EM  199910
EW  19991002
AB  Chemokines are believed to play a role in the neuropathogenesis
of AIDS
    through their recruitment of neurotoxin-secreting, virally infected
    leukocytes into the CNS. Levels of chemokines are elevated in
brains of
    patients and macaques with HIV/SIV-induced encephalitis. The
chemokine
    receptors CCR3, CCR5, and CXCR4 are found on subpopulations
of neurons in
    the cortex of human and macaque brain. We have developed an in
vitro
    system using both macaque and human fetal neurons and astrocytes
to
    further investigate the roles of these receptors in  ***neuronal***
    response to inflammation. Here we report the presence of
functional
    HIV/SIV coreceptors CCR3, CCR5, and CXCR4 on fetal human
and macaque
    neurons and CCR5 and CXCR4 on astrocytes immediately ex
***vivo***  and
    after several weeks in culture. Confocal imaging of immunostained
neurons
    demonstrated different patterns of distribution for these receptors,
which
    may have functional implications. Chemokine receptors were
shown to
    respond to their appropriate chemokine ligands with increases in
    intracellular calcium that, in the case of neurons, required
    predepolarization with KCl. These responses were blocked by
neutralizing
    chemokine receptor in mAbs. Pretreatment of neural cells with
pertussis
     ***toxin***  abolished responses to stromal-derived
factor-1alpha,
    macrophage inflammatory protein-1beta, and RANTES, indicating
coupling of
    CCR5 and CXCR4 to a Gialpha protein, as in leukocytes. Cultured
macaque
    neurons demonstrated calcium flux response to treatment with
recombinant
    SIVmac239 envelope protein, suggesting a mechanism by which
viral envelope
    could affect  ***neuronal***  function in SIV infection. The
presence of
    functional chemokine receptors on neurons and astrocytes suggests
that
    chemokines could serve to link inflammatory and  ***neuronal***

    responses.

L4  ANSWER 2 OF 18  MEDLINE
AN  1999253888    MEDLINE
DN  99253888
TI  GDNF: a novel factor with therapeutic potential for
```

neurodegenerative
disorders.
AU Walton K M
CS Department of Neurobiology, Cephalon, Inc., West Chester, PA 19380, USA.
SO MOLECULAR NEUROBIOLOGY, (1999 Feb) 19 (1) 43-59.
Journal code: AH6. ISSN: 0893-7648.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199908
AB The identification of novel factors that promote ***neuronal***
survival could have profound effects on developing new therapeutics for
neurodegenerative disorders. Glial cell line-derived neurotrophic factor
(GDNF) is a novel protein purified and cloned based on its marked ability
to promote dopaminergic ***neuronal*** function. GDNF, now known to be
the first identified member of a family of factors, signals through the
previously known receptor tyrosine kinase, Ret. Unlike most ligands for
receptor tyrosine kinases, GDNF does not bind and activate Ret directly,
but requires the presence of GPI-linked coreceptors. There are several
coreceptors with differing affinities for the GDNF family members. The
profile of coreceptors in a cell may determine which factor preferentially
activates Ret. In ***vivo*** differences in localization of the GDNF
family members, its coreceptors and Ret suggest this ligand/receptor
interaction has extensive and multiple functions in the CNS as well as in
peripheral tissues. GDNF promotes survival of several ***neuronal***
populations both in vitro and in ***vivo*** . Dopaminergic ***neuronal*** survival and function are preserved by GDNF in
***vivo*** when challenged by the ***toxins*** MPTP and
6-hydroxydopamine. Furthermore, GDNF improves the symptoms of
pharmacologically induced Parkinson's disease in monkeys. Several motor
neuron populations isolated in vitro are also rescued by GDNF. In
***vivo*** , GDNF protects these neurons from programmed cell death
associated with development and death induced by ***neuronal***
transection. These experiments suggest that GDNF may provide significant
therapeutic opportunities in several neurodegenerative disorders.

L4 ANSWER 3 OF 18 MEDLINE
AN 1999198837 MEDLINE
DN 99198837
TI Melatonin receptor potentiation of cyclic AMP and the cystic fibrosis
transmembrane conductance regulator ion channel.
AU Nelson C S; Marino J L; Allen C N
CS Center for Research on Occupational and Environmental Toxicology,
Department of Psychiatry, Oregon Health Sciences University, Portland
97201, USA.
NC AG10794 (NIA)
SO JOURNAL OF PINEAL RESEARCH, (1999 Mar) 26 (2) 113-21.
Journal code: JND. ISSN: 0742-3098.
CY Denmark
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199907
EW 19990704
AB We have used the cystic fibrosis transmembrane conductance regulator
(CFTR) Cl- channel as a model system to study the cAMP signal
***transduction*** pathways coupled to the Xenopus melatonin receptor.
During forskolin (Fsk) stimulation, melatonin reduced the amplitude of the
CFTR currents in oocytes injected with in vitro transcribed cRNAs for the
Xenopus melatonin receptor and CFTR. Pertussis ***toxin*** (Ptx)
treatment eliminated melatonin inhibition of Fsk stimulated CFTR currents.
In oocytes injected with cRNA for melatonin receptors, serotonin receptors
(5-HT7), and CFTR Cl- channels, application of melatonin together with
serotonin (5-HT) activated an additional inward current showing
potentiation of adenylyl cyclases by melatonin receptors. Subthreshold
activation of 5-HT7 receptors was sufficient and necessary to permit
activation of CFTR channels by melatonin. Preexposure to melatonin
desensitized the melatonin receptor mediated response. Therefore, based on
this model system, the effects of melatonin in ***vivo*** could be
either positive or negative modulation of other ***neuronal*** inputs,
depending on the mode of adenylyl cyclase stimulation.

L4 ANSWER 4 OF 18 MEDLINE
AN 1999192822 MEDLINE
DN 99192822
TI Non-viral ***neuronal*** gene delivery mediated by the HC fragment of
tetanus ***toxin*** .
AU Knight A; Carvajal J; Schneider H; Coutelle C; Chamberlain S; Fairweather
N
CS Section of Molecular Genetics, ICSM, London, UK.. am.knight@ic.ac.uk
SO EUROPEAN JOURNAL OF BIOCHEMISTRY, (1999 Feb) 259 (3) 762-9.
Journal code: EMZ. ISSN: 0014-2956.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199906
EW 19990604
AB Many inherited neurological diseases and cancers could potentially benefit
from efficient targeted gene delivery to neurons of the central nervous
system. The nontoxic fragment C (HC) of tetanus ***toxin*** retains
the specific nerve cell binding and transport properties of tetanus
holotoxin. The HC fragment has previously been used to promote the uptake
of attached proteins such as horseradish peroxidase, beta-galactosidase
and superoxide dismutase into ***neuronal*** cells in vitro and in
***vivo*** . We report the use of purified recombinant HC fragment
produced in yeast and covalently bound to polylysine [poly(K)] to enable
binding of DNA. We demonstrate that when used to ***transfect***
cells, this construct results in nonviral gene delivery and marker gene
expression in vitro in N18 RE 105 cells (a neuroblastoma x glioma
mouse/rat hybrid cell line) and F98 (a glioma cell line).
***Transfection*** was dependent on HC and was ***neuronal*** cell
type specific. HC may prove a useful targeting ligand for future
***neuronal*** gene therapy.

L4 ANSWER 5 OF 18 MEDLINE
AN 1999126974 MEDLINE
DN 99126974
TI Pituitary adenylate cyclase activating peptide (PACAP) in the retinohypothalamic tract: a daytime regulator of the biological clock.
AU Hannibal J; Ding J M; Chen D; Fahrenkrug J; Larsen P J; Gillette M U;
Mikkelsen J D
CS Department of Clinical Biochemistry, Bispebjerg Hospital,

University of
Copenhagen, Denmark.. biochbbh@inet.uni2.dk
NC NS22155 (NINDS)
SO ANNALS OF THE NEW YORK ACADEMY OF SCIENCES, (1998 Dec 11) 865 197-206.
Journal code: 5NM. ISSN: 0077-8923.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199904
EW 19990403
AB The retinohypothalamic tract (RHT) relays photic information from the eyes
to the brain biological clock in the suprachiasmatic nucleus (SCN).
Activation of this pathway by light plays a role in adjusting circadian
timing to light exposure at night. Here we report a new signaling pathway
by which the RHT regulates circadian timing in the daytime as well. Using
dual-immunocytochemistry for PACAP and the in ***vivo*** tracer
Cholera ***toxin*** subunit B (ChB), intense PACAP immunoreactivity
(PACAP-IR) was observed in retinal afferents at the rat SCN as well as in
the intergeniculate leaflet (IGL) of the thalamus. This PACAP-IR was
nearly lost upon bilateral eye enucleation. PACAP afferents originated
from ganglion cells distributed throughout the retina. The phase of
circadian rhythm measured as SCN ***neuronal*** activity in vitro was
significantly advanced by application of PACAP-38 during the subjective
day, but not at night. The effect is channelled to the clock via a PACAP 1
receptor-cAMP signaling mechanism. Thus, in addition to its role in
nocturnal regulation by glutamatergic neurotransmission, the RHT can
adjust the biological clock by a PACAP-cAMP-dependent mechanism during the
daytime.

L4 ANSWER 6 OF 18 MEDLINE
AN 1999066984 MEDLINE
DN 99066984
TI LIF (AM424), a promising growth factor for the treatment of ALS.
AU Kurek J B; Radford A J; Crump D E; Bower J J; Feeney S J; Austin L; Byrne
E
CS AMRAD Corporation Ltd, Melbourne, Australia.. jkurek@amrad.com.au
SO JOURNAL OF THE NEUROLOGICAL SCIENCES, (1998 Oct) 160 Suppl 1 S106-13.
Ref: 64
Journal code: JBJ. ISSN: 0022-510X.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199905
EW 19990503
AB Growth factors are theoretically promising agents for ALS therapy, but
have been disappointing in subcutaneous delivery due to either toxicity or
lack of major efficacy. Leukaemia inhibitory factor (LIF), was named after
its effect on haemopoietic cells, and belongs to a group of cytokines
which includes CNTF, IL-6, CT-1, OM and IL-11. All group members use the
gp130 signal ***transducing*** subunit for intracellular signalling,
but show differences in biological effect. In vitro and in ***vivo***
studies on axotomy and nerve crush models demonstrate a powerful effect of
LIF in the survival of both motor and sensory neurones, while reducing
denervation induced muscle atrophy. Its effects in muscle also include
stimulating myoblast proliferation in vitro, and up-regulation after
muscle injury. LIF will also stimulate muscle regeneration in ***vivo***
when applied exogenously after injury. In published studies of both
axotomy induced ***neuronal*** death and in the Wobbler mouse models
LIF is active at doses of 10 microg/kg delivered systemically, well below
the expected maximum tolerated dose suggested by primate safety studies.
LIF is expressed in low levels by spinal cord neurones with significant
up-regulation when the neurones are damaged by BOAA ***toxin*** , an
excitatory amino acid associated with a form of ALS. This augments other
evidence suggesting LIF is a trauma factor playing a role in the injury
response of adult ***neuronal*** tissue, and may be more effective
than related growth factors. Taken together, the data suggests LIF is a
physiologically relevant trophic factor with implications in clinical
medicine as a therapy for ALS, and a human recombinant form (AM424),
entered human clinical trials during 1998.

L4 ANSWER 7 OF 18 MEDLINE
AN 1998453369 MEDLINE
DN 98453369
TI Landmarks in the application of 13C-magnetic resonance spectroscopy to
studies of ***neuronal*** /glial relationships.
AU Bachelard H
CS MR Centre, Department of Physics, University of Nottingham, UK..
ppzwkp@ppn1.nott.ac.uk
SO DEVELOPMENTAL NEUROSCIENCE, (1998) 20 (4-5) 277-88. Ref: 70
Journal code: EC5. ISSN: 0378-5866.
CY Switzerland
DT (LECTURES)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199903
EW 19990301
AB The development of the use of carbon isotopes as metabolic tracers is
briefly described. 13C-labelled precursors (13CO2, 13CH4) first became
available in 1940 and were studied in microorganisms, but their use was
limited by very low enrichments and lack of suitable analytical equipment.
More success was achieved with 11C and especially 14C, as these
radioactive tracers did not need to be highly enriched. Although the
stable 13C isotope can be used at a low percentage enrichment in mass
spectrometry, its application to magnetic resonance spectroscopy (MRS)
requires very highly enriched precursors, due to its low natural abundance
and low sensitivity. Despite such limitations, however, the great
advantage of 13C-MRS lies in its exquisite chemical specificity, in that
labelling of different carbon atoms can be distinguished within the same
molecule. Effective exploitation became feasible in the early 1970s with
the advent of stable instruments, Fourier ***transform*** 13C-MRS, and
the availability of highly enriched precursors. Reports of its use in
brain research began to appear in the mid-1980s. The applications of 13C
isotopomer analysis to research on ***neuronal*** /glial relationships
are reviewed. The presence of neighbouring 13C-labelled atoms affects the
appearance of the resonances (splitting due to C-C coupling), and so
allows for unique quantification of rates through different and possibly

competing pathways. Isotopomer patterns in resonances labelled from a combination of [1-13C]glucose and [1, 2-13C2]acetate have revealed aspects of ***neuronal*** /glial metabolic trafficking on depolarization and under hypoxic conditions in vitro. This approach has now been applied to in ***vivo*** studies on inhibition of glial metabolism using fluoroacetate. The results confirm the glial specificity of the ***toxin*** and demonstrate that it does not affect entry of acetate. When the glial TCA cycle is inhibited, the ability of the glia to participate in the glutamate/glutamine cycle remains unimpaired, in that labelling of glutamine, which can only be derived from ***neuronal*** metabolism of glucose, persists. The results also confirmed earlier evidence that part of the GABA transmitter pool is derived from glial glutamine.

L4 ANSWER 8 OF 18 MEDLINE
AN 1998082844 MEDLINE
DN 98082844
TI Contributions of N-linked glycosylation to the expression of a functional alpha7-nicotinic receptor in Xenopus oocytes.
AU Chen D; Dang H; Patrick J W
CS Division of Neuroscience, Baylor College of Medicine, Houston, Texas 77030, USA.
NC NS13546 (NINDS)
DA04077 (NIDA)
SO JOURNAL OF NEUROCHEMISTRY, (1998 Jan) 70 (1) 349-57.
Journal code: JAV. ISSN: 0022-3042.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199804
EW 19980401
AB The alpha7 subunit of the ***neuronal*** nicotinic acetylcholine receptor, when expressed in Xenopus oocytes, forms homooligomeric ligand-gated ion channels that are blocked by a snake ***toxin*** , alpha-bungarotoxin. The amino-terminal extracellular domain of the alpha7 sequence has three consensus sites for asparagine-linked glycosylation (N46DS, N90MS, and N133AS). In this study, we show that alpha7 expressed either in ***vivo*** or in vitro is a glycoprotein of 57 kDa. In addition, we demonstrate by site-directed mutagenesis that all three consensus sites are used for glycosylation. To elucidate the role(s) of asparagine-linked glycosylation in the formation and function of the alpha7 receptor, wild-type and glycosylation-deficient alpha7 subunits were expressed in COS cells and oocytes. We examined biochemical and physiological properties of expressed receptors and found that alpha7 glycosylation mutations do not affect homooligomerization and surface protein expression of the alpha7 receptor but do affect surface expression of alpha-bungarotoxin binding sites and the function of the receptor. Our data indicate that asparagine-linked glycosylation is required for the expression of a functional alpha7 receptor in oocytes.

L4 ANSWER 9 OF 18 MEDLINE
AN 97360054 MEDLINE
DN 97360054
TI Neurotoxicity of soluble macrophage products in vitro--influence of dexamethasone.
AU Flavin M P; Ho L T; Coughlin K
CS Department of Pediatrics, Queen's University, Kingston, Ontario, Canada.
SO EXPERIMENTAL NEUROLOGY, (1997 Jun) 145 (2 Pt 1) 462-70.
Journal code: EQF. ISSN: 0014-4886.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199710
EW 19971001
AB When macrophage conditioned medium is added to neurons in vitro, there is a loss of cell membrane integrity, a loss of cell processes, and a large increase in apoptotic neurons. We tested the influence of a potent anti-inflammatory steroid on the interaction between macrophages and neurons. Dexamethasone was applied to macrophages in culture for 24 h while the culture was stimulated with lipopolysaccharide and hypoxia. Conditioned medium was collected after dexamethasone was removed. The dexamethasone pretreated medium was not toxic to hippocampal neurons in contrast to medium from stimulated macrophages not treated with steroid. The dexamethasone effect was concentration dependent. Pretreatment of macrophages with indomethacin and ***transforming*** growth factor beta had similar but less impressive effects when compared to dexamethasone. The effect of dexamethasone may have been mediated by inhibiting the synthesis or release of neurotoxic macrophage protein(s), as a combination of medium from steroid pretreated macrophages with medium from nontreated macrophages was not neuroprotective. The ***toxin*** (s) did not appear to be tumor necrosis factor alpha or arginase. A role for most neutral proteases was also excluded. We also assessed the consequence of stressing neurons with a mild hypoxic exposure immediately prior to conditioned medium application. Medium from dexamethasone-treated macrophages did not exaggerate hypoxic ***neuronal*** injury, unlike medium from non-dexamethasone-treated macrophages. It did not, however, block the exaggerating effect when coapplied in equal volume with medium from nontreated macrophages. Dexamethasone at 100 nM had no impact when applied directly to neurons while they were being exposed to conditioned medium. This in vitro protection by dexamethasone may be relevant to the demonstrated benefit of glucocorticoids in selected brain and spinal cord conditions. Suspicion of a potential link between this in vitro finding and in ***vivo*** CNS injury justifies an assessment of more specific agents acting on macrophage protein synthesis or secretion.

L4 ANSWER 10 OF 18 MEDLINE
AN 97218291 MEDLINE
DN 97218291
TI Pituitary adenylate cyclase-activating peptide (PACAP) in the retinohypothalamic tract: a potential daytime regulator of the biological clock.
AU Hannibal J; Ding J M; Chen D; Fahrenkrug J; Larsen P J; Gillette M U; Mikkelsen J D
CS Department of Clinical Biochemistry, Bispebjerg Hospital, University of Copenhagen, DK-2400 Copenhagen NV, Denmark.
NC NS22155 (NINDS)
SO JOURNAL OF NEUROSCIENCE, (1997 Apr 1) 17 (7) 2637-44.
Journal code: JDF. ISSN: 0270-6474.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals

EM 199904
EW 19990404
AB The retinohypothalamic tract (RHT) relays photic information from the eyes to the suprachiasmatic nucleus (SCN). Activation of this pathway by light plays a role in adjusting circadian timing via a glutamatergic pathway at night. Here we report a new signaling pathway by which the RHT may regulate circadian timing in the daytime as well. We used dual immunocytochemistry for pituitary adenylate cyclase-activating peptide (PACAP) and the in ***vivo*** tracer cholera ***toxin*** subunit B and observed intense PACAP-immunoreactivity (PACAP-IR) in retinal afferents in the rat SCN as well as in the intergeniculate leaflet (IGL) of the thalamus. This PACAP-IR in the SCN as well as in the IGL was nearly lost after bilateral eye enucleation. PACAP afferents originated from small ganglion cells distributed throughout the retina. The phase of circadian rhythm measured as SCN ***neuronal*** activity in vitro was significantly advanced (3.5 +/- 0.4 hr) by application of 1 x 10(-6) M PACAP-38 during the subjective day [circadian time (CT)-6] but not at night (CT14 and CT19). The phase-shifting effect is channeled to the clock via a PACAP-R1 receptor, because mRNA from this receptor was demonstrated in the ventral SCN by in situ hybridization. Furthermore, vasoactive intestinal peptide was nearly 1000-fold less potent in stimulating a phase advance at CT6. The signaling mechanism was through a cAMP-dependent pathway, which could be blocked by a specific cAMP antagonist, Rp-cAMPS. Thus, in addition to its role in nocturnal regulation by glutamatergic neurotransmission, the RHT may adjust the biological clock by a PACAP/cAMP-dependent mechanism during the daytime.

L4 ANSWER 11 OF 18 MEDLINE
AN 97157369 MEDLINE
DN 97157369
TI Calcium in suramin-induced rat sensory neuron toxicity in vitro.
AU Sun X; Windebank A J
CS Department of Neurology, Mayo Clinic and Mayo Foundation, Rochester, MN 55905, USA.
NC NS29769 (NINDS)
SO BRAIN RESEARCH, (1996 Dec 2) 742 (1-2) 149-56.
Journal code: B5L. ISSN: 0006-8993.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199706
EW 19970604
AB Suramin is an experimental chemotherapeutic agent and a neurotoxin which causes a dose-dependent peripheral neuropathy in ***vivo*** and inhibits dorsal root ganglion (DRG) neurite outgrowth in vitro. The mechanism of suramin-induced cyto- and neurotoxicity remains unclear. Calcium is a key signal ***transducer*** in cellular responses to a variety of physiological and pathogenic stimuli. In the present study, we have determined the role of calcium in suramin-induced neurotoxicity in dorsal root ganglion neurons in vitro. Suramin-induced inhibition of neurite outgrowth and induction of ***neuronal*** cell death were dose-related phenomena. A low level of extracellular calcium significantly reduced suramin-induced inhibition of neurite outgrowth and delayed ***neuronal*** cell death in vitro. Nimodipine (100 microM), an L-type voltage-sensitive calcium channel (VSCC) inhibitor, mimicked low calcium medium and protected neurite outgrowth in regular calcium medium supplemented with 300 microM suramin. TMB-8 (100 microM), an inhibitor of intracellular calcium release, failed to protect neurite outgrowth against the ***toxin*** . Calmidazolium (10 microM), a potent calmodulin inhibitor, and calpain inhibitor peptide (CIP, 10 microM) protected neurite outgrowth against suramin. The results support the hypothesis that the calcium signaling system is important in suramin-induced neurotoxicity. Influx of extracellular calcium is more important than release of intracellular calcium in causing cell injury in vitro.

L4 ANSWER 12 OF 18 MEDLINE
AN 96375823 MEDLINE
DN 96375823
TI Vasoactive intestinal polypeptide modulation of nicotinic ACh receptor channels in rat intracardiac neurones.
AU Cuevas J; Adams D J
CS Department of Molecular and Cellular Pharmacology, University of Miami, School of Medicine, FL 33101, USA.
NC HL-35422 (NHLBI) HL-07188 (NHLBI)
SO JOURNAL OF PHYSIOLOGY, (1996 Jun 1) 493 ( Pt 2) 503-15.
Journal code: JQV. ISSN: 0022-3751.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199705
AB 1. The effects of vasoactive intestinal polypeptide (VIP) on isolated parasympathetic neurones of rat intracardiac ganglia were examined under voltage clamp using dialysed and perforated patch whole-cell and excised outside-out membrane patch recording configurations. 2. VIP reversibly potentiated nicotinic ACh-evoked whole-cell currents, with half-maximal potentiation (EC50) obtained with 260 pM VIP. However, VIP had no effect on muscarinic ACh-evoked currents, ATP-evoked currents, or depolarization-activated ionic currents in these neurones. 3. VIP-induced potentiation of nicotinic ACh-evoked whole-cell currents was observed following cell dialysis, and was inhibited reversibly by bath application of the VIP receptor-binding inhibitor L-8-K (5 microM) or the ***neuronal*** nicotinic receptor antagonist mecamylamine (3 microM). 4. The signal ***transduction*** pathway mediating VIP-induced potentiation of nicotinic ACh-evoked currents involves a guanine nucleotide-binding protein (G-protein) but not cyclic AMP. Intracellular application of 100 microM GDP-beta-S, or pre-incubation of neurones with pertussis ***toxin*** , inhibited VIP-induced potentiation of ACh-evoked whole-cell currents. 5. In outside-out membrane patches, co-application of ACh (4 microM) and VIP (4 nM) decreased the duration of closings between bursts and clusters of bursts of ACh single-channel activity relative to control (4 microM, ACh alone). VIP, however, did not alter single ACh receptor channel current amplitude, duration of closings and openings within a burst, or mean burst duration. 6. VIP-induced modification of nicotinic ACh receptor channel kinetics results in an increase in the open-channel probability which is sufficient to account for the VIP-mediated potentiation of nicotinic ACh-evoked whole-cell currents. 7. The potentiation of nicotinic ACh-evoked currents by VIP is

likely to account for the altered ***neuronal*** activity observed in
the mammalian intracardiac ganglia in ***vivo*** and consequent
changes in heart rate and cardiac contractility.

L4 ANSWER 13 OF 18 MEDLINE
AN 95344784 MEDLINE
DN 95344784
TI Pertussis ***toxin*** specifically inhibits growth cone guidance by a
mechanism independent of direct G protein inactivation.
AU Kindt R M; Lander A D
CS Department of Biology, Massachusetts Institute of Technology, Cambridge
02139, USA.
SO NEURON, (1995 Jul) 15 (1) 79-88.
Journal code: AN8. ISSN: 0896-6273.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199511
AB An assay employing patterned laminin substrata was used to screen for
compounds that disrupt neurite guidance. One molecule, pertussis
***toxin*** , caused neurites to wander from patterns that normally
guided them, yet had no significant effect on rates of neurite outgrowth.
Wandering was greatest on patterns requiring frequent guidance (e.g.,
laminin stripes with periodic gaps). Surprisingly, the B oligomer of
pertussis ***toxin*** , which lacks the subunit that inactivates G
proteins, was equipotent at disrupting neurite guidance. Pertussis
***toxin*** probably acts by binding cell surface carbohydrates, since
neurites lacking complex-type N-linked oligosaccharides were insensitive
to the effects of the ***toxin*** . The B oligomer also blocked growth
cone collapse induced by a brain membrane-derived factor; such factors are
thought to act as repulsive guidance cues in ***vivo*** . That a single
reagent can inhibit ***neuronal*** responses to both attractive and
repulsive guidance cues suggests that such cues may share signaling pathways.

L4 ANSWER 14 OF 18 MEDLINE
AN 95179327 MEDLINE
DN 95179327
TI Fast inhibition of inwardly rectifying K+ channels by multiple neurotransmitter receptors in oligodendroglia.
AU Karschin A; Wischmeyer E; Davidson N; Lester H A
CS Max-Planck-Institute for Biophysical Chemistry, Gottingen, Germany.
NC GM-29836 (NIGMS)
SO EUROPEAN JOURNAL OF NEUROSCIENCE, (1994 Nov 1) 6 (11) 1756-64.
Journal code: BYG. ISSN: 0953-816X.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199506
AB An essential function of myelinating oligodendroglia in the mammalian
central nervous system is the regulation of extracellular potassium levels
by means of a prominent inwardly rectifying K+ current. Cardiac and
***neuronal*** K+ inward rectifiers are either activated by
hyperpolarizing voltages or controlled by neurotransmitters through the
action of receptor-activated G proteins. Neuromodulation of inward
rectifiers has not previously been considered as a way to regulate
oligodendrocyte function. Here we report the expression of serotonin,
somatostatin and muscarinic acetylcholine G protein-coupled receptors in
rat brain oligodendrocytes. Activation of these receptors leads to
pertussis ***toxin*** -sensitive inhibition of inwardly rectifying K+
channels within < 1 s. By contrast, in the heart and in neurons, similar
pathways activate an inwardly rectifying conductance. Thus,
transmitter-mediated blockade of inward rectifiers appears to be an
oligodendrocyte-specific variation of a common motif for convergent
signalling pathways. In ***vivo*** , expression of this mechanism,
which may be dependent on neuron-glia signalling, may have a regulatory
role in K+ homeostasis during neuron activity in the central nervous system.

L4 ANSWER 15 OF 18 MEDLINE
AN 94191900 MEDLINE
DN 94191900
TI In vitro labeling strategies for identifying primary neural tissue and a
***neuronal*** cell line after transplantation in the CNS.
AU Onifer S M; White L A; Whittemore S R; Holets V R
CS Department of Cell Biology and Anatomy, University of Miami School of
Medicine, FL 33136.
NC NS26887 (NINDS)
NS07044-16 (NINDS)
SO CELL TRANSPLANTATION, (1993 Mar-Apr) 2 (2) 131-49.
Journal code: B02. ISSN: 0963-6897.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199407
AB Potential labels for identifying embryonic raphe neurons and a clonal,
neuronally differentiating, raphe-derived cell line, RN33B, in CNS
transplantation studies were tested by first characterizing the labels in
vitro. The labels that were tested included 4',6-diamidino-2-phenylindole
hydrochloride, 1,1'-dioctadecyl-3,3,3'-tetramethylindocarbocyanine
perchlorate, the Escherichia coli lacZ gene, Fast Blue, Fluoro-Gold,
fluorescein-conjugated latex microspheres, fluorescein
isothiocyanate-conjugated or nonconjugated Phaseolus vulgaris
leucoagglutinin, methyl o-(6-amino-3'-imino-3H-xanthen-9-yl) benzoate
monohydrochloride, or tetanus ***toxin*** C fragment. Subsequently,
the optimal in vitro labels for embryonic raphe neurons and for RN33B
cells were characterized in ***vivo*** after CNS transplantation. In
vitro, 1,1'-dioctadecyl-3,3,3'-tetramethylindocarbocyanine perchlorate
(DiI) optimally labeled embryonic neurons. The Escherichia coli lacZ gene
optimally labeled RN33B cells. Most labels were rapidly diluted in
cultures of embryonic astrocytes and proliferating RN33B cells. Some
labels were toxic and were often retained in cellular debris. In
***vivo*** , DiI was visualized in transplanted, DiI-labeled raphe
neurons, but not in astrocytes up to 1 mo posttransplant. DiI-labeled host
cells were seen after transplantation of lysed, DiI-labeled cells.
beta-Galactosidase was visualized in transplanted, Escherichia coli lacZ
gene-labeled RN33B cells after 15 days in ***vivo*** . No
beta-galactosidase was seen in host cells after transplantation of lysed,
lacZ-labeled RN33B cells. The results demonstrate that labels for use in
CNS transplantation studies should be optimized for the specific
population of donor cells under study, with the initial step being
characterization in vitro followed by in ***vivo*** analysis.
Appropriate controls for false-positive labeling of host cells should always be assessed.

L4 ANSWER 16 OF 18 MEDLINE
AN 94170397 MEDLINE
DN 94170397
TI Platelet-activating factor: a putative neuromodulator and mediator in the
pathophysiology of brain injury.
AU Yue T L; Feuerstein G Z
CS Department of Cardiovascular Pharmacology, SmithKline Beecham

Pharmaceuticals, King of Prussia, PA 19406-0939.
SO CRITICAL REVIEWS IN NEUROBIOLOGY, (1994) 8 (1-2) 11-24. Ref: 88
Journal code: CRR. ISSN: 0892-0915.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199406
AB Platelet-activating factor (1-O-hexadecyl-2-acetyl-sn-glycero-3-phosphocholine [PAF]) is a potent lipid autocoid produced by many cell types. PAF is produced by cultured rat cerebellar neurons and human fetal brain cells, and has been extracted from brain tissue. Multiple PAF receptors have been demonstrated in brain tissue. PAF stimulates intracellular Ca2+ mobilization and phosphatidylinositol (PI) metabolism in ***transformed*** ***neuronal*** cell lines via the PAF receptor, to which both pertussis ***toxin*** (PTX)-sensitive and -insensitive G protein appear to couple. PAF has potent actions on cerebral vessels and cerebral metabolism when administered in ***vivo*** . Direct ***neuronal*** effects of PAF, such as inhibition of acetylcholine release, are observed in vitro. Excessive PAF production in pathological states of the nervous system, such as neurotrauma and stroke, has been shown. In multiple studies in rodent and non-rodent models using highly specific and potent PAF antagonists, reversal or prevention of key consequences of brain injury, such as hypoperfusion following ischemia, reperfusion and edema, inflammatory cell accumulation, neurologic/motor deficits, and ***neuronal*** salvage, has been demonstrated. These studies taken together support a role for PAF as an important mediator in the pathophysiology of brain injury.

L4 ANSWER 17 OF 18 MEDLINE
AN 94037127 MEDLINE
DN 94037127
TI Metabolic mapping with cellular resolution: c-fos vs. 2-deoxyglucose.
AU Sharp F R; Sagar S M; Swanson R A
CS Department of Neurology, University of California at San Francisco..
NC NS27864 (NINDS)
NS27488 (NINDS)
SO CRITICAL REVIEWS IN NEUROBIOLOGY, (1993) 7 (3-4) 205-28. Ref: 159
Journal code: CRR. ISSN: 0892-0915.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LA English
FS Priority Journals
EM 199402
AB 2-Deoxyglucose (2DG) studies have been most useful in mapping activated regions of the nervous system. Cellular localization studies using 2DG have been less rewarding, but results are consistent with current views that increases of 2DG accumulation produced by synaptic activation represent increases in glycolytic glucose metabolism occurring mainly in presynaptic ***neuronal*** and possibly glial elements. Immediate early genes (IEGs), including the fos, jun, and NGFI-A families, are induced by a wide variety of intracellular signaling pathways. The nuclear localization of the protein products of these genes and their induction by a variety of stimuli make them useful in metabolic activation studies carried out at the cellular level. IEGs have been induced in neurons by osmotic, bacterial endotoxin, steroids, stress, and other hormonal stimuli; by light, auditory, painful, and other sensory stimuli; during stimulation of motor cortex and other motor behaviors; and by various drugs and ***toxins*** that act on a variety of neurotransmitter systems, including dopamine and glutamate. In addition, the localization of c-fos gene expression identifies cells that respond to growth factors in ***vivo*** . Retinal Muller cells, the major glial cell type of the retina, demonstrate nuclear Fos immunostaining after the intravitreal injection of epidermal growth factor (EGF) or ***transforming*** growth factor-alpha (TGF-alpha). This observation demonstrates that adult glia can respond to these growth factors in ***vivo*** . The investigation of early response gene expression may be particularly useful for elucidating the role of trophic factors in the cellular response to central nervous system injury.

L4 ANSWER 18 OF 18 MEDLINE
AN 92343492 MEDLINE
DN 92343492
TI NMDA receptor-mediated arachidonic acid release in neurons: role in signal ***transduction*** and pathological aspects.
AU Lazarewicz J W; Salinska E; Wroblewski J T
CS Fidia-Georgetown Institute for the Neurosciences, Georgetown University School of Medicine, Washington DC.
SO ADVANCES IN EXPERIMENTAL MEDICINE AND BIOLOGY, (1992) 318 73-89.
Journal code: 2LU. ISSN: 0065-2598.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199210
AB The N-methyl-D-aspartate (NMDA)-sensitive subtype of glutamate receptor, which gates Ca(2+)-permeable ion channels, is known for its role in learning and memory formation, in the induction of long-term potentiation, and also in seizure activity and neurotoxicity. In primary cultures of cerebellar neurons, agonists of NMDA receptors induce a dose-dependent release of [3H]arachidonic acid ([3H]AA), which is potentiated by activation of the glycine-positive modulatory site and inhibited by NMDA receptor antagonists. NMDA receptor-induced [3H]AA release is inhibited by quinacrine and partially depends on the presence of extracellular calcium. The [3H]AA release is not sensitive, however, to pretreatment with pertussis or cholera ***toxin*** , which suggests a Ca(2+)-dependent activation of phospholipase A2 not employing G proteins. Pretreatment of cultures with the natural and semisynthetic sphingolipids GT1b and PKS 3, respectively, inhibits NMDA receptor-mediated [3H]AA release. We also demonstrated glutamate-evoked [3H]AA release from rat hippocampal slices, which is NMDA receptor mediated, calcium dependent and sensitive to quinacrine. Arachidonic acid and its metabolites have been shown to play a role as second messengers and to modulate ***neuronal*** activity. Moreover, they are thought to act as transsynaptic modulators in the mechanism of NMDA receptor-induced long-term potentiation in the hippocampus. Their role in ischemic brain pathology has also been postulated. Our experiments on cultured cerebellar granule cells, incubated in a Mg(2+)-free medium deprived of glucose and oxygen, demonstrated a time-dependent stimulation of [3H]AA release. This release was inhibited by antagonists of NMDA receptors and by quinacrine. Stimulation of NMDA-sensitive glutamate receptors and the subsequent

calcium-mediated activation of phospholipase A2 may play a role in the in
***vivo*** release of arachidonic acid during brain ischemia. This
hypothesis is supported by the observation that the enhanced level of
thromboxane B2 in the gerbil brain after 5 min of global ischemia is
reduced by the systemic application of either the NMDA antagonist MK-801
or the ganglioside GM1.

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FILE 'MEDLINE' ENTERED AT 09:24:53 ON 21 SEP 2000
L1 80711 S NEURONAL/AB,BI
L2 5827 S L1 AND (TRANSFECT? OR TRANSFORM? OR TRANSDUC?)/AB,BI
L3 180 S L2 AND TOXIN#/AB,BI
L4 18 S L3 AND VIVO/AB,BI

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49585 ONCOGENE/BI
5413360 AB/FA
14886 ONCOGENE/AB
(ONCOGENE/BI (L) AB/FA)
49585 ONCOGENE/BI
L5 9 L3 AND ONCOGENE/AB,BI

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YOU HAVE REQUESTED DATA FROM 9 ANSWERS - CONTINUE? Y/(N):y

L5 ANSWER 1 OF 9 MEDLINE
AN 2000312858 MEDLINE
DN 20312858
TI ***Neuronal*** apoptosis induced by pharmacological concentrations of
3-hydroxykynurenine: characterization and protection by dantrolene and
Bcl-2 overexpression.
AU Wei H; Leeds P; Chen R W; Wei W; Leng Y; Bredesen D E; Chuang D M
CS Section on Molecular Neurobiology, Biological Psychiatry Branch, National
Institute of Mental Health, National Institutes of Health, Bethesda, Maryland, USA.
SO JOURNAL OF NEUROCHEMISTRY, (2000 Jul) 75 (1) 81-90.
Journal code: JAV. ISSN: 0022-3042.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200009
EW 20000904
AB We have studied neurotoxicity induced by pharmacological concentrations of
3-hydroxykynurenine (3-HK), an endogenous ***toxin*** implicated in
certain neurodegenerative diseases, in cerebellar granule cells, PC12
pheochromocytoma cells, and GT1-7 hypothalamic neurosecretory cells. In
all three cell types, the toxicity was induced in a dose-dependent manner
by 3-HK at high micromolar concentrations and had features characteristic
of apoptosis, including chromatin condensation and internucleosomal DNA
cleavage. In cerebellar granule cells, the 3-HK neurotoxicity was
unaffected by xanthine oxidase inhibitors but markedly potentiated by
superoxide dismutase and its hemelike mimetic, MnTBAP [manganese(III)
tetrakis(benzoic acid)porphyrin chloride]. Catalase blocked 3-HK
neurotoxicity in the absence and presence of superoxide dismutase or
MnTBAP. The formation of H(2)O(2) was demonstrated in PC12 and GT1-7 cells
treated with 3-HK, by measuring the increase in the fluorescent product,
2',7'-dichlorofluorescein. In both PC12 and cerebellar granule cells,
inhibitors of the neutral amino acid transporter that mediates the uptake
of 3-HK failed to block 3-HK toxicity. However, their toxicity was
slightly potentiated by the iron chelator, deferoxamine. Taken together,
our results suggest that neurotoxicity induced by pharmacological
concentrations of 3-HK in these cell types is mediated primarily by
H(2)O(2), which is formed most likely by auto-oxidation of 3-HK in
extracellular compartments. 3-HK-induced death of PC12 and GT1-7 cells was
protected by dantrolene, an inhibitor of calcium release from the
endoplasmic reticulum. The protection by dantrolene was associated with a
marked increase in the protein level of Bcl-2, a prominent antiapoptotic
gene product. Moreover, overexpression of Bcl-2 in GT1-7 cells elicited by
gene ***transfection*** suppressed 3-HK toxicity. Thus, dantrolene may
elicit its neuroprotective effects by mechanisms involving up-regulation
of the level and function of Bcl-2 protein.

L5 ANSWER 2 OF 9 MEDLINE
AN 1999402800 MEDLINE
DN 99402800
TI Neurite extension occurs in the absence of regulated exocytosis in PC12
subclones.
AU Leoni C; Menegon A; Benfenati F; Toniolo D; Pennuto M; Valtorta F
CS San Raffaele Scientific Institute, Consiglio Nazionale delle Richerche
Center for Cellular and Molecular Pharmacology and B. Ceccarelli Center
for Neurobiology, University of Milan, Milan, Italy.
SO MOLECULAR BIOLOGY OF THE CELL, (1999 Sep) 10 (9) 2919-31.
Journal code: BAU. ISSN: 1059-1524.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199912
AB We have investigated the process leading to differentiation of PC12 cells.
This process is known to include extension of neurites and changes in the
expression of subsets of proteins involved in cytoskeletal rearrangements
or in neurosecretion. To this aim, we have studied a PC12 clone (trk-PC12)
stably ***transfected*** with the nerve growth factor receptor TrkA.
These cells are able to undergo both spontaneous and neurotrophin-induced
morphological differentiation. However, both undifferentiated and nerve
growth factor-differentiated trk-PC12 cells appear to be completely
defective in the expression of proteins of the secretory apparatus,
including proteins of synaptic vesicles and large dense-core granules,
neurotransmitter transporters, and neurotransmitter-synthesizing enzymes.
These results indicate that neurite extension can occur independently of
the presence of the neurosecretory machinery, including the proteins that
constitute the fusion machine, suggesting the existence of differential
activation pathways for the two processes during ***neuronal***
differentiation. These findings have been confirmed in independent clones
obtained from PC12-27, a previously characterized PC12 variant clone
globally incompetent for regulated secretion. In contrast, the integrity
of the Rab cycle appears to be necessary for neurite extension, because
antisense oligonucleotides against the neurospecific isoform of
Rab-guanosine diphosphate-dissociation inhibitor significantly interfere

with process formation.

L5 ANSWER 3 OF 9 MEDLINE
AN 1999253888 MEDLINE
DN 99253888
TI GDNF: a novel factor with therapeutic potential for neurodegenerative
disorders.
AU Walton K M
CS Department of Neurobiology, Cephalon, Inc., West Chester, PA 19380, USA.
SO MOLECULAR NEUROBIOLOGY, (1999 Feb) 19 (1) 43-59.
Journal code: AH6. ISSN: 0893-7648.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199908
AB The identification of novel factors that promote ***neuronal***
survival could have profound effects on developing new therapeutics for
neurodegenerative disorders. Glial cell line-derived neurotrophic factor
(GDNF) is a novel protein purified and cloned based on its marked ability
to promote dopaminergic ***neuronal*** function. GDNF, now known to be
the first identified member of a family of factors, signals through the
previously known receptor tyrosine kinase, Ret. Unlike most ligands for
receptor tyrosine kinases, GDNF does not bind and activate Ret directly,
but requires the presence of GPI-linked coreceptors. There are several
coreceptors with differing affinities for the GDNF family members. The
profile of coreceptors in a cell may determine which factor preferentially
activates Ret. In vivo differences in localization of the GDNF family
members, its coreceptors and Ret suggest this ligand/receptor interaction
has extensive and multiple functions in the CNS as well as in peripheral
tissues. GDNF promotes survival of several ***neuronal*** populations
both in vitro and in vivo. Dopaminergic ***neuronal*** survival and
function are preserved by GDNF in vivo when challenged by the
***toxins*** MPTP and 6-hydroxydopamine. Furthermore, GDNF improves the
symptoms of pharmacologically induced Parkinson's disease in monkeys.
Several motor neuron populations isolated in vitro are also rescued by
GDNF. In vivo, GDNF protects these neurons from programmed cell death
associated with development and death induced by ***neuronal***
transection. These experiments suggest that GDNF may provide significant
therapeutic opportunities in several neurodegenerative disorders.

L5 ANSWER 4 OF 9 MEDLINE
AN 1998389793 MEDLINE
DN 98389793
TI mu-Opioid receptor activates signaling pathways implicated in cell
survival and translational control.
AU Polakiewicz R D; Schieferl S M; Gingras A C; Sonenberg N; Comb M J
CS Cell Signaling Laboratory, New England Biolabs, Beverly, Massachusetts
01915, USA.
NC DA05706 (NIDA)
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1998 Sep 4) 273 (36) 23534-41.
Journal code: HIV. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199812
AB The mu-opioid receptor mediates the analgesic and addictive properties of
morphine. Despite the clinical importance of this G-protein-coupled
receptor and many years of pharmacological research, few intracellular
signaling mechanisms triggered by morphine and other mu-opioid agonists
have been described. We report that mu-opioid agonists stimulate three
different effectors of a phosphoinositide 3-kinase (PI3K)-dependent
signaling cascade. By using a cell line stably ***transfected*** with
the mu-opioid receptor cDNA, we show that the specific agonist
[D-Ala2,N-Me-Phe4,Gly5-ol]enkephalin (DAMGO) stimulates the activity of
Akt, a serine/threonine protein kinase implicated in protecting neurons
from apoptosis. Activation of Akt by DAMGO correlates with its
phosphorylation at serine 473. The selective PI3K inhibitors wortmannin
and LY294002 blocked phosphorylation of this site, previously shown to be
necessary for Akt enzymatic activity. DAMGO also stimulates the
phosphorylation of two other downstream effectors of PI3K, the p70 S6
kinase and the repressors of mRNA translation, 4E-BP1 and 4E-BP2. Upon
mu-opioid receptor stimulation, p70 S6 kinase is activated and
phosphorylated at threonine 389 and at threonine 421/serine 424.
Phosphorylation of p70 S6 kinase and 4E-BP1 is also repressed by PI3K
inhibitors as well as by rapamycin, the selective inhibitor of FRAP/mTOR.
Consistent with these findings, DAMGO-stimulated phosphorylation of 4E-BP1
impairs its ability to bind the translation initiation factor eIF-4E.
These results demonstrate that the mu-opioid receptor activates signaling
pathways associated with ***neuronal*** survival and translational
control, two processes implicated in ***neuronal*** development and
synaptic plasticity.

L5 ANSWER 5 OF 9 MEDLINE
AN 1998355475 MEDLINE
DN 98355475
TI Complement C5a anaphylatoxin fragment causes apoptosis in TGW
neuroblastoma cells.
AU Farkas I; Baranyi L; Liposits Z S; Yamamoto T; Okada H
CS Department of Molecular Biology, Nagoya City University School of
Medicine, Nagoya, Japan.
SO NEUROSCIENCE, (1998 Oct) 86 (3) 903-11.
Journal code: NZR. ISSN: 0306-4522.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199901
EW 19990104
AB Human neuroblastoma TGW cells express a C5a anaphylatoxin receptor-like
molecule termed ***neuronal*** C5a receptor. A C5a-receptor fragment
peptide (termed PR226-multiple antigenic peptide) can induce rapid
apoptosis in TGW cells via ***neuronal*** C5a receptor-associated
signal ***transduction*** pathways. In order to analyse role of
activated complement system in neurodegeneration, TGW cells were exposed
to an oligomer form of a C5a fragment (amino acids: 37-53) peptide termed
PL37-multiple antigenic peptide. Upon treatment with PL37-multiple
antigenic peptide, an increased nuclear c-fos expression was shown within
30 min. DNA fragmentation, a hallmark of apoptosis, was noted within 4 h.
Extracellular administration of 100 nM PL37-multiple antigenic peptide
evoked inward calcium current pulses. At higher doses (0.5 microM-1

microM), PL37-multiple antigenic peptide evoked higher current pulses,
followed by an irreversible, high inward current. To exert its apoptotic
effect, PL37-multiple antigenic peptide utilizes a pertussis ***toxin***
-sensitive signal ***transduction*** pathway associated with the
***neuronal*** C5a receptor. Activation of the complement system and
therefore release of C5a has already been reported in Alzheimer's disease.
In addition, the presence of the Kunitz-type proteinase inhibitors
indicates an impaired protease function and a possible abnormal
fragmentation of C5a anaphylatoxin. Our data suggest that neurons
expressing ***neuronal*** C5a receptor are more vulnerable to the
apoptosis associated with the ***neuronal*** C5a receptor and the
possibility that abnormal activation of C5a receptor and C5a anaphylatoxin
fragments might be involved in the pathogenesis of Alzheimer's disease.

L5 ANSWER 6 OF 9 MEDLINE
AN 1998177184 MEDLINE
DN 98177184
TI A ***neuronal*** C5a receptor and an associated apoptotic signal
***transduction*** pathway.
AU Farkas I; Baranyi L; Takahashi M; Fukuda A; Liposits Z; Yamamoto T; Okada
H
CS Department of Molecular Biology, Nagoya City University School of
Medicine, Nagoya 467, Japan.
SO JOURNAL OF PHYSIOLOGY, (1998 Mar 15) 507 ( Pt 3) 679-87.
Journal code: JQV. ISSN: 0022-3751.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199807
AB 1. We report the first experimental evidence of a ***neuronal*** C5a
receptor (nC5aR) in human cells of ***neuronal*** origin. Expression
of nC5aR mRNA was demonstrated by the reverse transcriptase-polymerase
chain reaction (RT-PCR) in TGW human neuroblastoma cells. 2. Expression of
a functional C5aR was supported by the finding that C5a evoked a transient
increase in the intracellular calcium level as measured by flow cytometry
(FACS). 3. To analyse the function of the nC5aR, an antisense peptide
fragment of the C5aR was used. Previous data showed that a C5aR fragment
(a peptide termed PR226) has C5aR agonist and antagonist effects in U-937
cells depending on the concentration of the peptide. We found that a
multiple antigenic peptide (MAP) form of the same peptide (termed
PR226-MAP) induced rapid elevation of nuclear c-fos immunoreactivity and
resulted in DNA fragmentation, a characteristic sign of apoptosis, in TGW
cells. 4. Early electrophysiological events characteristic of apoptosis
were also detected: intermittent calcium current pulses were recorded
within 1-2 min of peptide administration. C5a pretreatment delayed the
onset of this calcium influx. 5. We also demonstrated that the apoptotic
pathway is linked to nC5aR via pertussis ***toxin*** -sensitive
G-proteins. 6. Although the function of C5a and its receptor on neurons is
unknown, these results suggest that an abnormal activation of this signal
***transduction*** pathway can result in apoptosis and, subsequently, in
neurodegeneration.

L5 ANSWER 7 OF 9 MEDLINE
AN 94037127 MEDLINE
DN 94037127
TI Metabolic mapping with cellular resolution: c-fos vs. 2-deoxyglucose.
AU Sharp F R; Sagar S M; Swanson R A
CS Department of Neurology, University of California at San Francisco..
NC NS27864 (NINDS)
NS27488 (NINDS)
SO CRITICAL REVIEWS IN NEUROBIOLOGY, (1993) 7 (3-4) 205-28. Ref: 159
Journal code: CRR. ISSN: 0892-0915.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LA English
FS Priority Journals
EM 199402
AB 2-Deoxyglucose (2DG) studies have been most useful in mapping activated
regions of the nervous system. Cellular localization studies using 2DG
have been less rewarding, but results are consistent with current views
that increases of 2DG accumulation produced by synaptic activation
represent increases in glycolytic glucose metabolism occurring mainly in
presynaptic ***neuronal*** and possibly glial elements. Immediate
early genes (IEGs), including the fos, jun, and NGFI-A families, are
induced by a wide variety of intracellular signaling pathways. The nuclear
localization of the protein products of these genes and their induction by
a variety of stimuli make them useful in metabolic activation studies
carried out at the cellular level. IEGs have been induced in neurons by
osmotic, bacterial endotoxin, steroids, stress, and other hormonal
stimuli; by light, auditory, painful, and other sensory stimuli; during
stimulation of motor cortex and other motor behaviors; and by various
drugs and ***toxins*** that act on a variety of neurotransmitter
systems, including dopamine and glutamate. In addition, the localization
of c-fos gene expression identifies cells that respond to growth factors
in vivo. Retinal Muller cells, the major glial cell type of the retina,
demonstrate nuclear Fos immunostaining after the intravitreal injection of
epidermal growth factor (EGF) or ***transforming*** growth
factor-alpha (TGF-alpha). This observation demonstrates that adult glia
can respond to these growth factors in vivo. The investigation of early
response gene expression may be particularly useful for elucidating the
role of trophic factors in the cellular response to central nervous system
injury.

L5 ANSWER 8 OF 9 MEDLINE
AN 90150622 MEDLINE
DN 90150622
TI Small molecular weight GTP-binding proteins and signal
***transduction*** .
AU Yamamoto K; Tanimoto T; Kim S; Kikuchi A; Takai Y
CS Department of Biochemistry, Kobe University School of Medicine, Japan.
SO CLINICA CHIMICA ACTA, (1989 Dec 15) 185 (3) 347-55.
Journal code: DCC. ISSN: 0009-8981.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199005
AB We have separated multiple GTP-binding proteins (G proteins) having Mr
values of about 20,000 (small Mr G proteins) from bovine brain membranes,
purified to near homogeneity and characterized two novel G proteins

designated as smg p25A and smg p21, the c-Ki-ras protein (c-Ki-ras p21)
and the two rho proteins (rho p20 and rho p21). smg p25A is present
abundantly in brain and adrenal medulla. This G protein is also found in
rat pheochromocytoma PC-12 cells, and its mRNA level increased after
differentiation of the cells into neuron-like cells in response to nerve
growth factor or dibutyryl cyclic AMP. These results suggest that smg p25A
plays an important role in the regulation of ***neuronal*** functions.
In contrast, smg p21 is found in most tissues. This G protein has the same
putative effector domain as ras p21s, suggesting that smg p21 exerts the
actions similar and/or antagonistic to those of ras p21s. In fact, smg p21
has been found to be identical with the protein encoded by the Krev-1 gene
recently isolated as a gene suppressing the ***transforming*** action
of Ki-ras p21 in NIH/3T3 cells. On the other hand, rho p20 and rho p21 are
ADP-ribosylated by an ADP-ribosyltransferase contained or contaminated in
botulinum ***toxin*** type C1, presumably C3. Botulinum
ADP-ribosyltransferase C3 has recently been shown to induce morphological
changes similar to those induced by ras p21 in fibroblasts. Thus, small Mr
G proteins are part of a huge network of intracellular regulatory systems
and play important roles in the regulation of various cell functions
including cell ***transformation*** , proliferation and
differentiation.

L5 ANSWER 9 OF 9 MEDLINE
AN 90040817 MEDLINE
DN 90040817
TI Differentiation of PC12 cells with v-src: comparison with nerve growth
factor.
AU Rausch D M; Dickens G; Doll S; Fujita K; Koizumi S; Rudkin B B; Tocco M;
Eiden L E; Guroff G
CS Unit on Molecular and Cellular Neurobiology, National Institute of Mental
Health, Bethesda, MD 20892.
SO JOURNAL OF NEUROSCIENCE RESEARCH, (1989 Sep) 24 (1) 49-58.
Journal code: KAC. ISSN: 0360-4012.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199002
AB The PC12 rat pheochromocytoma cell line is used extensively as a model to
study ***neuronal*** differentiation. These cells resemble adrenal
chromaffin cells, differentiating both morphologically and biochemically
when cultured in the presence of dexamethasone, but develop a sympathetic
neuron-like phenotype when cultured in the presence of nerve growth
factor. Expression of the protein product of the v-src ***oncogene***
in PC12 cells also induces neurite outgrowth similar to that resulting
from nerve growth factor treatment (Alema et al: Nature 316:557-559,
1985). It is thus possible that c-src or a src-like tyrosine kinase
participates in the signal ***transduction*** pathway by which nerve
growth factor acts on PC12 cells. In this study a temperature-sensitive
v-src gene has been introduced into PC12 cells. When cultures of these
src- ***transformed*** cells are switched from the nonpermissive (40
degrees C) to the permissive (37 degrees C) temperature they elaborate
neurites. The differentiation induced by src has been compared with that
induced by nerve growth factor by determining whether src-
***transformed*** PC12 cells at 37 degrees C exhibit the same
biochemical alterations as those induced in PC12 cells treated with nerve
growth factor. Neurite extension at 37 degrees C in v-src-
***transformed*** cells, like NGF-induced differentiation, is
accompanied by an increase in the nerve growth factor-inducible large
external (NILE) protein. However, neurite extension in v-src-
***transformed*** cells is not blocked by the protein kinase inhibitor
K-252a, which completely blocks NGF-induced neurite extension. Likewise,
EGF receptor down-regulation and the development of saxitoxin and tetanus
***toxin*** binding sites are either much reduced or completely absent
in src-differentiated compared with NGF-differentiated PC12 cells.

=> d his

(FILE 'HOME' ENTERED AT 09:24:45 ON 21 SEP 2000)

FILE 'MEDLINE' ENTERED AT 09:24:53 ON 21 SEP 2000

L1 80711 S NEURONAL/AB,BI
L2 5827 S L1 AND (TRANSFECT? OR TRANSFORM? OR TRANSDUC?)/AB,BI
L3 180 S L2 AND TOXIN#/AB,BI
L4 18 S L3 AND VIVO/AB,BI
L5 9 S L3 AND ONCOGENE/AB,BI

=> s l5 and vivo/ab,bi

267353 VIVO/BI
5413360 AB/FA
230827 VIVO/AB
(VIVO/BI (L) AB/FA)
267353 VIVO/BI
L6 2 L5 AND VIVO/AB,BI

=> d l- bib ab

YOU HAVE REQUESTED DATA FROM 2 ANSWERS - CONTINUE? Y/(N):y

L6 ANSWER 1 OF 2 MEDLINE
AN 1999253888 MEDLINE
DN 99253888
TI GDNF: a novel factor with therapeutic potential for neurodegenerative
disorders.
AU Walton K M
CS Department of Neurobiology, Cephalon, Inc., West Chester, PA 19380, USA.
SO MOLECULAR NEUROBIOLOGY, (1999 Feb) 19 (1) 43-59.
Journal code: AH6. ISSN: 0893-7648.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199908
AB The identification of novel factors that promote ***neuronal***
survival could have profound effects on developing new therapeutics for
neurodegenerative disorders. Glial cell line-derived neurotrophic factor
(GDNF) is a novel protein purified and cloned based on its marked ability
to promote dopaminergic ***neuronal*** function. GDNF, now known to be
the first identified member of a family of factors, signals through the
previously known receptor tyrosine kinase, Ret. Unlike most ligands for
receptor tyrosine kinases, GDNF does not bind and activate Ret directly,
but requires the presence of GPI-linked coreceptors. There are several
coreceptors with differing affinities for the GDNF family members.

The
profile of coreceptors in a cell may determine which factor preferentially
activates Ret. In ***vivo*** differences in localization of the GDNF
family members, its coreceptors and Ret suggest this ligand/receptor
interaction has extensive and multiple functions in the CNS as well as in
peripheral tissues. GDNF promotes survival of several ***neuronal***
populations both in vitro and in ***vivo*** . Dopaminergic
***neuronal*** survival and function are preserved by GDNF in
***vivo*** when challenged by the ***toxins*** MPTP and
6-hydroxydopamine. Furthermore, GDNF improves the symptoms of
pharmacologically induced Parkinson's disease in monkeys. Several motor
neuron populations isolated in vitro are also rescued by GDNF. In
***vivo*** , GDNF protects these neurons from programmed cell death
associated with development and death induced by ***neuronal***
transection. These experiments suggest that GDNF may provide significant
therapeutic opportunities in several neurodegenerative disorders.

L6 ANSWER 2 OF 2 MEDLINE
AN 94037127 MEDLINE
DN 94037127
TI Metabolic mapping with cellular resolution: c-fos vs. 2-deoxyglucose.
AU Sharp F R; Sagar S M; Swanson R A
CS Department of Neurology, University of California at San Francisco..
NC NS27864 (NINDS)
NS27488 (NINDS)
SO CRITICAL REVIEWS IN NEUROBIOLOGY, (1993) 7 (3-4) 205-28. Ref: 159
Journal code: CRR. ISSN: 0892-0915.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LA English
FS Priority Journals
EM 199402
AB 2-Deoxyglucose (2DG) studies have been most useful in mapping activated
regions of the nervous system. Cellular localization studies using 2DG
have been less rewarding, but results are consistent with current views
that increases of 2DG accumulation produced by synaptic activation
represent increases in glycolytic glucose metabolism occurring mainly in
presynaptic ***neuronal*** and possibly glial elements. Immediate
early genes (IEGs), including the fos, jun, and NGFI-A families, are
induced by a wide variety of intracellular signaling pathways. The nuclear
localization of the protein products of these genes and their induction by
a variety of stimuli make them useful in metabolic activation studies
carried out at the cellular level. IEGs have been induced in neurons by
osmotic, bacterial endotoxin, steroids, stress, and other hormonal
stimuli; by light, auditory, painful, and other sensory stimuli; during
stimulation of motor cortex and other motor behaviors; and by various
drugs and ***toxins*** that act on a variety of neurotransmitter
systems, including dopamine and glutamate. In addition, the localization
of c-fos gene expression identifies cells that respond to growth factors
in ***vivo*** . Retinal Muller cells, the major glial cell type of the
retina, demonstrate nuclear Fos immunostaining after the intravitreal
injection of epidermal growth factor (EGF) or ***transforming***
growth factor-alpha (TGF-alpha). This observation demonstrates that adult
glia can respond to these growth factors in ***vivo*** . The
investigation of early response gene expression may be particularly useful
for elucidating the role of trophic factors in the cellular response to
central nervous system injury.

=> s l3 and tumorigenic and vivo/ab,bi

5288 TUMORIGENIC
267353 VIVO/BI
5413360 AB/FA
230827 VIVO/AB
(VIVO/BI (L) AB/FA)
267353 VIVO/BI
L7 0 L3 AND TUMORIGENIC AND VIVO/AB,BI

=> s l3 and tumorigenic/ab,bi

5288 TUMORIGENIC/BI
5413360 AB/FA
4972 TUMORIGENIC/AB
(TUMORIGENIC/BI (L) AB/FA)
5288 TUMORIGENIC/BI
L8 0 L3 AND TUMORIGENIC/AB,BI

=> s l3 and immortaliz?/ab,bi

5479 IMMORTALIZ?/BI
5413360 AB/FA
5078 IMMORTALIZ?/AB
(IMMORTALIZ?/BI (L) AB/FA)
5479 IMMORTALIZ?/BI
L9 2 L3 AND IMMORTALIZ?/AB,BI

=> d l- bib ab

YOU HAVE REQUESTED DATA FROM 2 ANSWERS - CONTINUE? Y/(N):y

L9 ANSWER 1 OF 2 MEDLINE
AN 1999427870 MEDLINE
DN 99427870
TI Bradykinin receptor localization and cell signaling pathways used by.
bradykinin in the regulation of gonadotropin-releasing hormone secretion.
AU Shi B; Bhat G; Mahesh V B; Brotto M; Nosek T M; Brann D W
CS Department of Physiology and Endocrinology, Medical College of Georgia,
Augusta 30912, USA.
NC HD-28964 (NICHD)
SO ENDOCRINOLOGY, (1999 Oct) 140 (10) 4669-76.
Journal code: EGZ. ISSN: 0013-7227.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 199912
EW 19991203
AB In a previous publication we provided evidence of a novel ***neuronal***
pathway for the control of GnRH secretion by bradykinin. The action of
bradykinin appeared to be exerted through the bradykinin B2 receptor. In
this study we demonstrated that the bradykinin B2 receptor is densely
localized in the arcuate nucleus, median eminence, organum vasculosum of
the lamina terminalis, and preoptic area, regions known to be critical for
the control of GnRH secretion. To determine the mechanism of action of
bradykinin in stimulating GnRH release, we used ***immortalized***
GnRH (GT1-7) cells in vitro. Bradykinin stimulation of GnRH secretion from
GT1-7 cells appears to involve activation of the phospholipase C signaling
pathway and mobilization of extracellular and intracellular calcium
stores. Evidence to support this contention was derived from the
observations that incubation of the phospholipase C inhibitor,

U-73122
with bradykinin, blocked the ability of bradykinin to stimulate release
from GT1-7 cells. This effect was specific, as a nitric oxide synthase
inhibitor and a cyclooxygenase inhibitor were found to have no effect on
bradykinin-induced GnRH secretion, suggesting that nitric oxide and PGs do
not mediate bradykinin effects. Pertussis ***toxin*** also had no
effect on bradykinin action. This suggests that the bradykinin B2 receptor
may be coupled to a pertussis ***toxin*** -insensitive G protein in
GT1-7 cells. With respect to calcium involvement in bradykinin action,
fura-2 calcium indicator studies revealed that bradykinin can rapidly
increase intracellular Ca2+ levels in GT1-7 cells. A role for
intracellular Ca2+ in bradykinin action was further suggested by the
finding that an intracellular calcium chelator, 1,2-bis(O-aminophenoxy)]ethane-N,N,N',N'-tetraacetic acid tetraacetoxymethyl ester,
significantly attenuated the effects of bradykinin on GnRH release. The
elevation of intracellular calcium by bradykinin appears to be due to
mobilization of calcium from the endoplasmic reticulum, as incubation of
the Ca2+-adenosine triphosphatase inhibitor thapsigarin, which depletes
endoplasmic reticulum Ca2+ stores, significantly attenuated bradykinin
action on GnRH release. Extracellular calcium may also be involved in
bradykinin action, as the L-type Ca2+ channel blockers verapamil and
nifedipine had no effect on bradykinin-induced GnRH release, whereas the
nonselective Ca2+ channel blocker, nickel chloride, attenuated
bradykinin-induced GnRH release. Taken as a whole, these studies
demonstrate that the bradykinin B2 receptor is densely localized in key
hypothalamic nuclei responsible for regulation of GnRH release, and that
the mechanism of bradykinin stimulation of GnRH secretion involves
activation of the phospholipase C signaling pathway, with a critical role
implicated for calcium in bradykinin action in GT1-7 cells.

L9 ANSWER 2 OF 2 MEDLINE
AN 1998378489 MEDLINE
DN 98378489
TI Nicotinic receptor-induced apoptotic cell death of hippocampal progenitor
cells.
AU Berger F; Gage F H; Vijayaraghavan S
CS Laboratory of Genetics, The Salk Institute, La Jolla, California 92037,
USA.
SO JOURNAL OF NEUROSCIENCE, (1998 Sep 1) 18 (17) 6871-81.
Journal code: JDF. ISSN: 0270-6474.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199811
EW 19981102
AB Nicotine has many effects on CNS functions, presumably through its action
on ***neuronal*** nicotinic acetylcholine receptors (AChRs). One
subclass of AChRs that binds the snake venom ***toxin***
alpha-bungarotoxin (alpha-Bgt-AChRs) has been shown to modulate
neurotransmission in the brain. We now show that alpha-Bgt-AChR activation
by low doses of nicotine results in apoptotic cell death of both primary
and ***immortalized*** hippocampal progenitor cells. In HC2S2-
***immortalized*** hippocampal progenitors, nicotine is cytotoxic to
undifferentiated cells, whereas it spares the same cells once
differentiation has been induced. The activation of alpha-Bgt-AChRs by
nicotine results in the induction of the tumor suppressor protein p53 and
the cdk inhibitor p21. The cytotoxic effect of nicotine is dependent on
extracellular calcium levels and is probably attributable to the poor
ability of undifferentiated progenitors to buffer calcium loads. The major
calcium buffer in these cells, calbindin D28K, is present only after
differentiation has been induced. Furthermore ***transfection*** of
undifferentiated cells with calbindin results in dramatic protection
against the cytotoxic effects of nicotine. These results show that
nicotine abuse could have significant effects on the survival of
progenitor populations in the developing and adult brain and also suggest
an endogenous role for alpha-Bgt-AChRs in ***neuronal*** development
and differentiation.

=> d his

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FILE 'MEDLINE' ENTERED AT 09:24:53 ON 21 SEP 2000
L1 80711 S NEURONAL/AB,BI
L2 5827 S L1 AND (TRANSFECT? OR TRANSFORM? OR TRANSDUC?)/AB,BI
L3 180 S L2 AND TOXIN#/AB,BI
L4 18 S L3 AND VIVO/AB,BI
L5 9 S L3 AND ONCOGENE/AB,BI
L6 2 S L5 AND VIVO/AB,BI
L7 0 S L3 AND TUMORIGENIC AND VIVO/AB,BI
L8 0 S L3 AND TUMORIGENIC/AB,BI
L9 2 S L3 AND IMMORTALIZ?/AB,BI

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| FULL ESTIMATED COST | | 8.29 | 8.44 |

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3 FILES SEARCHED...
L10 19 L5 OR L6 OR L7 OR L8 OR L9

=> dup rem l10

PROCESSING COMPLETED FOR L10
L11 12 DUP REM L10 (7 DUPLICATES REMOVED)

=> d l- bib ab

YOU HAVE REQUESTED DATA FROM 12 ANSWERS - CONTINUE? Y/(N):y

L11 ANSWER 1 OF 12 MEDLINE
AN 2000312858 MEDLINE
DN 20312858
TI ***Neuronal*** apoptosis induced by pharmacological concentrations of
3-hydroxykynurenine: characterization and protection by dantrolene

and
Bcl-2 overexpression.
AU Wei H; Leeds P; Chen R W; Wei W; Leng Y; Bredesen D E; Chuang D M
CS Section on Molecular Neurobiology, Biological Psychiatry Branch, National
Institute of Mental Health, National Institutes of Health, Bethesda, Maryland, USA.
SO JOURNAL OF NEUROCHEMISTRY, (2000 Jul) 75 (1) 81-90.
Journal code: JAV. ISSN: 0022-3042.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200009
EW 20000904
AB We have studied neurotoxicity induced by pharmacological concentrations of
3-hydroxykynurenine (3-HK), an endogenous ***toxin*** implicated in
certain neurodegenerative diseases, in cerebellar granule cells, PC12
pheochromocytoma cells, and GT1-7 hypothalamic neurosecretory cells. In
all three cell types, the toxicity was induced in a dose-dependent manner
by 3-HK at high micromolar concentrations and had features characteristic
of apoptosis, including chromatin condensation and internucleosomal DNA
cleavage. In cerebellar granule cells, the 3-HK neurotoxicity was
unaffected by xanthine oxidase inhibitors but markedly potentiated by
superoxide dismutase and its hemelike mimetic, MnTBAP [manganese(III)
tetrakis(benzoic acid)porphyrin chloride]. Catalase blocked 3-HK
neurotoxicity in the absence and presence of superoxide dismutase or
MnTBAP. The formation of H(2)O(2) was demonstrated in PC12 and GT1-7 cells
treated with 3-HK, by measuring the increase in the fluorescent product,
2',7'-dichlorofluorescein. In both PC12 and cerebellar granule cells,
inhibitors of the neutral amino acid transporter that mediates the uptake
of 3-HK failed to block 3-HK toxicity. However, their toxicity was
slightly potentiated by the iron chelator, deferoxamine. Taken together,
our results suggest that neurotoxicity induced by pharmacological
concentrations of 3-HK in these cell types is mediated primarily by
H(2)O(2), which is formed most likely by auto-oxidation of 3-HK in
extracellular compartments. 3-HK-induced death of PC12 and GT1-7 cells was
protected by dantrolene, an inhibitor of calcium release from the
endoplasmic reticulum. The protection by dantrolene was associated with a
marked increase in the protein level of Bcl-2, a prominent antiapoptotic
gene product. Moreover, overexpression of Bcl-2 in GT1-7 cells elicited by
gene ***transfection*** suppressed 3-HK toxicity. Thus, dantrolene may
elicit its neuroprotective effects by mechanisms involving up-regulation
of the level and function of Bcl-2 protein.

L11 ANSWER 2 OF 12 MEDLINE DUPLICATE 1
AN 1999427870 MEDLINE
DN 99427870
TI Bradykinin receptor localization and cell signaling pathways used by
bradykinin in the regulation of gonadotropin-releasing hormone secretion.
AU Shi B; Bhat G; Mahesh V B; Brotto M; Nosek T M; Brann D W
CS Department of Physiology and Endocrinology, Medical College of Georgia,
Augusta 30912, USA.
NC HD-28964 (NICHD)
SO ENDOCRINOLOGY, (1999 Oct) 140 (10) 4669-76.
Journal code: EGZ. ISSN: 0013-7227.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 199912
EW 19991203
AB In a previous publication we provided evidence of a novel ***neuronal***
pathway for the control of GnRH secretion by bradykinin. The action of
bradykinin appeared to be exerted through the bradykinin B2 receptor. In
this study we demonstrated that the bradykinin B2 receptor is densely
localized in the arcuate nucleus, median eminence, organum vasculosum of
the lamina terminalis, and preoptic area, regions known to be critical for
the control of GnRH secretion. To determine the mechanism of action of
bradykinin in stimulating GnRH release, we used ***immortalized***
GnRH (GT1-7) cells in vitro. Bradykinin stimulation of GnRH secretion from
GT1-7 cells appears to involve activation of the phospholipase C signaling
pathway and mobilization of extracellular and intracellular calcium
stores. Evidence to support this contention was derived from the
observations that incubation of the phospholipase C inhibitor, U-73122
with bradykinin, blocked the ability of bradykinin to stimulate release
from GT1-7 cells. This effect was specific, as a nitric oxide synthase
inhibitor and a cyclooxygenase inhibitor were found to have no effect on
bradykinin-induced GnRH secretion, suggesting that nitric oxide and PGs do
not mediate bradykinin effects. Pertussis ***toxin*** also had no
effect on bradykinin action. This suggests that the bradykinin B2 receptor
may be coupled to a pertussis ***toxin*** -insensitive G protein in
GT1-7 cells. With respect to calcium involvement in bradykinin action,
fura-2 calcium indicator studies revealed that bradykinin can rapidly
increase intracellular Ca2+ levels in GT1-7 cells. A role for
intracellular Ca2+ in bradykinin action was further suggested by the
finding that an intracellular calcium chelator, 1,2-bis(O-
aminophenoxy)]ethane-N,N,N',N'-tetraacetic acid tetraacetoxymethyl ester,
significantly attenuated the effects of bradykinin on GnRH release. The
elevation of intracellular calcium by bradykinin appears to be due to
mobilization of calcium from the endoplasmic reticulum, as incubation of
the Ca2+-adenosine triphosphatase inhibitor thapsigarin, which depletes
endoplasmic reticulum Ca2+ stores, significantly attenuated bradykinin
action on GnRH release. Extracellular calcium may also be involved in
bradykinin action, as the L-type Ca2+ channel blockers verapamil and
nifedipine had no effect on bradykinin-induced GnRH release, whereas the
nonselective Ca2+ channel blocker, nickel chloride, attenuated
bradykinin-induced GnRH release. Taken as a whole, these studies
demonstrate that the bradykinin B2 receptor is densely localized in key
hypothalamic nuclei responsible for regulation of GnRH release, and that
the mechanism of bradykinin stimulation of GnRH secretion involves
activation of the phospholipase C signaling pathway, with a critical role
implicated for calcium in bradykinin action in GT1-7 cells.

L11 ANSWER 3 OF 12 MEDLINE
AN 1999402800 MEDLINE
DN 99402800
TI Neurite extension occurs in the absence of regulated exocytosis in PC12
subclones.
AU Leoni C; Menegon A; Benfenati F; Toniolo D; Pennuto M; Valtorta F
CS San Raffaele Scientific Institute, Consiglio Nazionale delle

Richerche
Center for Cellular and Molecular Pharmacology and B. Ceccarelli Center
for Neurobiology, University of Milan, Milan, Italy.
SO MOLECULAR BIOLOGY OF THE CELL, (1999 Sep) 10 (9) 2919-31.
Journal code: BAU. ISSN: 1059-1524.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199912
AB We have investigated the process leading to differentiation of PC12 cells.
This process is known to include extension of neurites and changes in the
expression of subsets of proteins involved in cytoskeletal rearrangements
or in neurosecretion. To this aim, we have studied a PC12 clone (trk-PC12)
stably ***transfected*** with the nerve growth factor receptor TrkA.
These cells are able to undergo both spontaneous and neurotrophin-induced
morphological differentiation. However, both undifferentiated and nerve
growth factor-differentiated trk-PC12 cells appear to be completely
defective in the expression of proteins of the secretory apparatus,
including proteins of synaptic vesicles and large dense-core granules,
neurotransmitter transporters, and neurotransmitter-synthesizing enzymes.
These results indicate that neurite extension can occur independently of
the presence of the neurosecretory machinery, including the proteins that
constitute the fusion machine, suggesting the existence of differential
activation pathways for the two processes during ***neuronal***
differentiation. These findings have been confirmed in independent clones
obtained from PC12-27, a previously characterized PC12 variant clone
globally incompetent for regulated secretion. In contrast, the integrity
of the Rab cycle appears to be necessary for neurite extension, because
antisense oligonucleotides against the neurospecific isoform of
Rab-guanosine diphosphate-dissociation inhibitor significantly interfere
with process formation.

L11 ANSWER 4 OF 12 MEDLINE
AN 1999253888 MEDLINE
DN 99253888
TI GDNF: a novel factor with therapeutic potential for neurodegenerative
disorders.
AU Walton K M
CS Department of Neurobiology, Cephalon, Inc., West Chester, PA 19380, USA.
SO MOLECULAR NEUROBIOLOGY, (1999 Feb) 19 (1) 43-59.
Journal code: AH6. ISSN: 0893-7648.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199908
AB The identification of novel factors that promote ***neuronal***
survival could have profound effects on developing new therapeutics for
neurodegenerative disorders. Glial cell line-derived neurotrophic factor
(GDNF) is a novel protein purified and cloned based on its marked ability
to promote dopaminergic ***neuronal*** function. GDNF, now known to be
the first identified member of a family of factors, signals through the
previously known receptor tyrosine kinase, Ret. Unlike most ligands for
receptor tyrosine kinases, GDNF does not bind and activate Ret directly,
but requires the presence of GPI-linked coreceptors. There are several
coreceptors with differing affinities for the GDNF family members. The
profile of coreceptors in a cell may determine which factor preferentially
activates Ret. In ***vivo*** differences in localization of the GDNF
family members, its coreceptors and Ret suggest this ligand/receptor
interaction has extensive and multiple functions in the CNS as well as in
peripheral tissues. GDNF promotes survival of several ***neuronal***
populations both in vitro and in ***vivo*** . Dopaminergic
***neuronal*** survival and function are preserved by GDNF in
***vivo*** when challenged by the ***toxins*** MPTP and
6-hydroxydopamine. Furthermore, GDNF improves the symptoms of
pharmacologically induced Parkinson's disease in monkeys. Several motor
neuron populations isolated in vitro are also rescued by GDNF. In
***vivo*** , GDNF protects these neurons from programmed cell death
associated with development and death induced by ***neuronal***
transection. These experiments suggest that GDNF may provide significant
therapeutic opportunities in several neurodegenerative disorders.

L11 ANSWER 5 OF 12 MEDLINE
AN 1998389793 MEDLINE
DN 98389793
TI mu-Opioid receptor activates signaling pathways implicated in cell survival and translational control.
AU Polakiewicz R D; Schieferl S M; Gingras A C; Sonenberg N; Comb M J
CS Cell Signaling Laboratory, New England Biolabs, Beverly, Massachusetts
01915, USA.
NC DA05706 (NIDA)
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1998 Sep 4) 273 (36) 23534-41.
Journal code: HIV. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199812
AB The mu-opioid receptor mediates the analgesic and addictive properties of
morphine. Despite the clinical importance of this G-protein-coupled
receptor and many years of pharmacological research, few intracellular
signaling mechanisms triggered by morphine and other mu-opioid agonists
have been described. We report that mu-opioid agonists stimulate three
different effectors of a phosphoinositide 3-kinase (PI3K)-dependent
signaling cascade. By using a cell line stably ***transfected*** with
the mu-opioid receptor cDNA, we show that the specific agonist
[D-Ala2,N-Me-Phe4,Gly5-ol]enkephalin (DAMGO) stimulates the activity of
Akt, a serine/threonine protein kinase implicated in protecting neurons
from apoptosis. Activation of Akt by DAMGO correlates with its
phosphorylation at serine 473. The selective PI3K inhibitors wortmannin
and LY294002 blocked phosphorylation of this site, previously shown to be
necessary for Akt enzymatic activity. DAMGO also stimulates the
phosphorylation of two other downstream effectors of PI3K, the p70 S6
kinase and the repressors of mRNA translation, 4E-BP1 and 4E-BP2. Upon
mu-opioid receptor stimulation, p70 S6 kinase is activated and
phosphorylated at threonine 389 and at threonine 421/serine 424.
Phosphorylation of p70 S6 kinase and 4E-BP1 is also repressed by PI3K
inhibitors as well as by rapamycin, the selective inhibitor of FRAP/mTOR.
Consistent with these findings, DAMGO-stimulated phosphorylation of 4E-BP1

impairs its ability to bind the translation initiation factor eIF-4E. These results demonstrate that the mu-opioid receptor activates signaling pathways associated with ***neuronal*** survival and translational control, two processes implicated in ***neuronal*** development and synaptic plasticity.

L11 ANSWER 6 OF 12 MEDLINE DUPLICATE 2
AN 1998378489 MEDLINE
DN 98378489
TI Nicotinic receptor-induced apoptotic cell death of hippocampal progenitor cells.
AU Berger F; Gage F H; Vijayaraghavan S
CS Laboratory of Genetics, The Salk Institute, La Jolla, California 92037, USA.
SO JOURNAL OF NEUROSCIENCE, (1998 Sep 1) 18 (17) 6871-81.
Journal code: JDF. ISSN: 0270-6474.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199811
EW 19981102
AB Nicotine has many effects on CNS functions, presumably through its action on ***neuronal*** nicotinic acetylcholine receptors (AChRs). One subclass of AChRs that binds the snake venom ***toxin*** alpha-bungarotoxin (alpha-Bgt-AChRs) has been shown to modulate neurotransmission in the brain. We now show that alpha-Bgt-AChR activation by low doses of nicotine results in apoptotic cell death of both primary and ***immortalized*** hippocampal progenitor cells. In HC2S2-***immortalized*** hippocampal progenitors, nicotine is cytotoxic to undifferentiated cells, whereas it spares the same cells once differentiation has been induced. The activation of alpha-Bgt-AChRs by nicotine results in the induction of the tumor suppressor protein p53 and the cdk inhibitor p21. The cytotoxic effect of nicotine is dependent on extracellular calcium levels and is probably attributable to the poor ability of undifferentiated progenitors to buffer calcium loads. The major calcium buffer in these cells, calbindin D28K, is present only after differentiation has been induced. Furthermore ***transfection*** of undifferentiated cells with calbindin results in dramatic protection against the cytotoxic effects of nicotine. These results show that nicotine abuse could have significant effects on the survival of progenitor populations in the developing and adult brain and also suggest an endogenous role for alpha-Bgt-AChRs in ***neuronal*** development and differentiation.

L11 ANSWER 7 OF 12 MEDLINE
AN 1998355475 MEDLINE
DN 98355475
TI Complement C5a anaphylatoxin fragment causes apoptosis in TGW neuroblastoma cells.
AU Farkas I; Baranyi L; Liposits Z S; Yamamoto T; Okada H
CS Department of Molecular Biology, Nagoya City University School of Medicine, Nagoya, Japan.
SO NEUROSCIENCE, (1998 Oct) 86 (3) 903-11.
Journal code: NZR. ISSN: 0306-4522.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199901
EW 19990104
AB Human neuroblastoma TGW cells express a C5a anaphylatoxin receptor-like molecule termed ***neuronal*** C5a receptor. A C5a-receptor fragment peptide (termed PR226-multiple antigenic peptide) can induce rapid apoptosis in TGW cells via ***neuronal*** C5a receptor-associated signal ***transduction*** pathways. In order to analyse role of activated complement system in neurodegeneration, TGW cells were exposed to an oligomer form of a C5a fragment (amino acids: 37-53) peptide termed PL37-multiple antigenic peptide. Upon treatment with PL37-multiple antigenic peptide, an increased nuclear c-fos expression was shown within 30 min. DNA fragmentation, a hallmark of apoptosis, was noted within 4 h. Extracellular administration of 100 nM PL37-multiple antigenic peptide evoked inward calcium current pulses. At higher doses (0.5 microM-1 microM), PL37-multiple antigenic peptide evoked higher current pulses, followed by an irreversible, high inward current. To exert its apoptotic effect, PL37-multiple antigenic peptide utilizes a pertussis ***toxin*** -sensitive signal ***transduction*** pathway associated with the ***neuronal*** C5a receptor. Activation of the complement system and therefore release of C5a has already been reported in Alzheimer's disease. In addition, the presence of the Kunitz-type proteinase inhibitors indicates an impaired protease function and a possible abnormal fragmentation of C5a anaphylatoxin. Our data suggest that neurons expressing ***neuronal*** C5a receptor are more vulnerable to the apoptosis associated with the ***neuronal*** C5a receptor and the possibility that abnormal activation of C5a receptor and C5a anaphylatoxin fragments might be involved in the pathogenesis of Alzheimer's disease.

L11 ANSWER 8 OF 12 MEDLINE
AN 1998177184 MEDLINE
DN 98177184
TI A ***neuronal*** C5a receptor and an associated apoptotic signal ***transduction*** pathway.
AU Farkas I; Baranyi L; Takahashi M; Fukuda A; Liposits Z; Yamamoto T; Okada H
CS Department of Molecular Biology, Nagoya City University School of Medicine, Nagoya 467, Japan.
SO JOURNAL OF PHYSIOLOGY, (1998 Mar 15) 507 ( Pt 3) 679-87.
Journal code: JQV. ISSN: 0022-3751.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199807
AB 1. We report the first experimental evidence of a ***neuronal*** C5a receptor (nC5aR) in human cells of ***neuronal*** origin. Expression of nC5aR mRNA was demonstrated by the reverse transcriptase-polymerase chain reaction (RT-PCR) in TGW human neuroblastoma cells. 2. Expression of a functional C5aR was supported by the finding that C5a evoked a transient increase in the intracellular calcium level as measured by flow cytometry (FACS). 3. To analyse the function of the nC5aR, an antisense peptide fragment of the C5aR was used. Previous data showed that a C5aR fragment (a peptide termed PR226) has C5aR agonist and antagonist effects in U-937 cells depending on the concentration of the peptide. We found that a

multiple antigenic peptide (MAP) form of the same peptide (termed
PR226-MAP) induced rapid elevation of nuclear c-fos immunoreactivity and
resulted in DNA fragmentation, a characteristic sign of apoptosis, in TGW
cells. 4. Early electrophysiological events characteristic of apoptosis
were also detected: intermittent calcium current pulses were recorded
within 1-2 min of peptide administration. C5a pretreatment delayed the
onset of this calcium influx. 5. We also demonstrated that the apoptotic
pathway is linked to nC5aR via pertussis ***toxin*** -sensitive
G-proteins. 6. Although the function of C5a and its receptor on neurons is
unknown, these results suggest that an abnormal activation of this signal
***transduction*** pathway can result in apoptosis and, subsequently, in
neurodegeneration.

L11 ANSWER 9 OF 12 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 96270797 EMBASE
DN 1996270797
TI Chronic opioid treatment induces adenylyl cyclase V superactivation.
Involvement of G(.beta..gamma.).
AU Avidor-Reiss T.; Nevo I.; Levy R.; Pfeuffer T.; Vogel Z.
CS Department of Neurobiology, Weizmann Institute of Science,76100 Rehovot,
Israel
SO Journal of Biological Chemistry, (1996) 271/35 (21309-21315).
ISSN: 0021-9258 CODEN: JBCHA3
CY United States
DT Journal; Article
FS 005 General Pathology and Pathological Anatomy
008 Neurology and Neurosurgery
029 Clinical Biochemistry
040 Drug Dependence, Alcohol Abuse and Alcoholism
LA English
SL English
AB It has been known for some time that chronic treatment of ***neuronal***
cells and tissues with opioids, contrary to their acute effect, leads to
an increase in cAMP accumulation. This phenomenon, defined as adenylyl
cyclase superactivation, has been implicated in opiate addiction, yet the
mechanism by which it is induced remains unclear. Here, we show that this
phenomenon can be reproduced and studied in COS-7 cells cotransfected with
adenylyl cyclase type V and .mu.-opioid receptor cDNAs. These cells
display acute opioid inhibition of adenylyl cyclase activity, whereas
prolonged exposure to the .mu.-agonist morphine or [D-Ala2, N-methyl-Phe4,
Gly-ol5]enkephalin leads to a time-dependent superactivation of adenylyl
cyclase. This superactivated state is reversible, because it is gradually
lost following agonist withdrawal. Adenylyl cyclase superactivation can be
prevented by pertussis ***toxin*** pretreatment, indicating the
involvement of G(i/o) proteins, or by cotransfection with the carboxyl
terminus of .beta.-adrenergic receptor kinase or with .alpha.-
***transducin*** (scavengers of G(.beta..gamma.) dimers), indicating a
role for the G protein .beta..gamma. dimers in adenylyl cyclase
superactivation. However, contrary to several other G(.beta..gamma.)-
dependent signal ***transduction*** mechanisms (e.g. the extracellular
signal-regulated kinase 2/MAP kinase pathway), adenylyl cyclase
superactivation is not affected by the Ras dominant negative mutant
N17-Ras.

L11 ANSWER 10 OF 12 MEDLINE DUPLICATE 3
AN 94037127 MEDLINE
DN 94037127
TI Metabolic mapping with cellular resolution: c-fos vs. 2-deoxyglucose.
AU Sharp F R; Sagar S M; Swanson R A
CS Department of Neurology, University of California at San Francisco..
NC NS27864 (NINDS)
NS27488 (NINDS)
SO CRITICAL REVIEWS IN NEUROBIOLOGY, (1993) 7 (3-4) 205-28. Ref: 159
Journal code: CRR. ISSN: 0892-0915.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LA English
FS Priority Journals
EM 199402
AB 2-Deoxyglucose (2DG) studies have been most useful in mapping activated
regions of the nervous system. Cellular localization studies using 2DG
have been less rewarding, but results are consistent with current views
that increases of 2DG accumulation produced by synaptic activation
represent increases in glycolytic glucose metabolism occurring mainly in
presynaptic ***neuronal*** and possibly glial elements. Immediate
early genes (IEGs), including the fos, jun, and NGFI-A families, are
induced by a wide variety of intracellular signaling pathways. The nuclear
localization of the protein products of these genes and their induction by
a variety of stimuli make them useful in metabolic activation studies
carried out at the cellular level. IEGs have been induced in neurons by
osmotic, bacterial endotoxin, steroids, stress, and other hormonal
stimuli; by light, auditory, painful, and other sensory stimuli; during
stimulation of motor cortex and other motor behaviors; and by various
drugs and ***toxins*** that act on a variety of neurotransmitter
systems, including dopamine and glutamate. In addition, the localization
of c-fos gene expression identifies cells that respond to growth factors
in ***vivo*** . Retinal Muller cells, the major glial cell type of the
retina, demonstrate nuclear Fos immunostaining after the intravitreal
injection of epidermal growth factor (EGF) or ***transforming***
growth factor-alpha (TGF-alpha). This observation demonstrates that adult
glia can respond to these growth factors in ***vivo*** . The
investigation of early response gene expression may be particularly useful
for elucidating the role of trophic factors in the cellular response to
central nervous system injury.

L11 ANSWER 11 OF 12 MEDLINE
AN 90150622 MEDLINE
DN 90150622
TI Small molecular weight GTP-binding proteins and signal ***transduction*** .
AU Yamamoto K; Tanimoto T; Kim S; Kikuchi A; Takai Y
CS Department of Biochemistry, Kobe University School of Medicine, Japan.
SO CLINICA CHIMICA ACTA, (1989 Dec 15) 185 (3) 347-55.
Journal code: DCC. ISSN: 0009-8981.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199005
AB We have separated multiple GTP-binding proteins (G proteins) having Mr
values of about 20,000 (small Mr G proteins) from bovine brain membranes,
purified to near homogeneity and characterized two novel G proteins
designated as smg p25A and smg p21, the c-Ki-ras protein (c-Ki-ras p21)
and the two rho proteins (rho p20 and rho p21). smg p25A is present

abundantly in brain and adrenal medulla. This G protein is also found in
rat pheochromocytoma PC-12 cells, and its mRNA level increased after
differentiation of the cells into neuron-like cells in response to nerve
growth factor or dibutyryl cyclic AMP. These results suggest that smg p25A
plays an important role in the regulation of ***neuronal*** functions.
In contrast, smg p21 is found in most tissues. This G protein has the same
putative effector domain as ras p21s, suggesting that smg p21 exerts the
actions similar and/or antagonistic to those of ras p21s. In fact, smg p21
has been found to be identical with the protein encoded by the Krev-1 gene
recently isolated as a gene suppressing the ***transforming*** action
of Ki-ras p21 in NIH/3T3 cells. On the other hand, rho p20 and rho p21 are
ADP-ribosylated by an ADP-ribosyltransferase contained or contaminated in
botulinum ***toxin*** type C1, presumably C3. Botulinum
ADP-ribosyltransferase C3 has recently been shown to induce morphological
changes similar to those induced by ras p21 in fibroblasts. Thus, small Mr
G proteins are part of a huge network of intracellular regulatory systems
and play important roles in the regulation of various cell functions
including cell ***transformation*** , proliferation and
differentiation.

L11 ANSWER 12 OF 12 MEDLINE DUPLICATE 4
AN 90040817 MEDLINE
DN 90040817
TI Differentiation of PC12 cells with v-src: comparison with nerve growth
factor.
AU Rausch D M; Dickens G; Doll S; Fujita K; Koizumi S; Rudkin B B; Tocco M;
Eiden L E; Guroff G
CS Unit on Molecular and Cellular Neurobiology, National Institute of Mental
Health, Bethesda, MD 20892.
SO JOURNAL OF NEUROSCIENCE RESEARCH, (1989 Sep) 24 (1) 49-58.
Journal code: KAC. ISSN: 0360-4012.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199002
AB The PC12 rat pheochromocytoma cell line is used extensively as a model to
study ***neuronal*** differentiation. These cells resemble adrenal
chromaffin cells, differentiating both morphologically and biochemically
when cultured in the presence of dexamethasone, but develop a sympathetic
neuron-like phenotype when cultured in the presence of nerve growth
factor. Expression of the protein product of the v-src ***oncogene***
in PC12 cells also induces neurite outgrowth similar to that resulting
from nerve growth factor treatment (Alema et al: Nature 316:557-559,
1985). It is thus possible that c-src or a src-like tyrosine kinase
participates in the signal ***transduction*** pathway by which nerve
growth factor acts on PC12 cells. In this study a temperature-sensitive
v-src gene has been introduced into PC12 cells. When cultures of these
src- ***transformed*** cells are switched from the nonpermissive (40
degrees C) to the permissive (37 degrees C) temperature they elaborate
neurites. The differentiation induced by src has been compared with that
induced by nerve growth factor by determining whether src-
***transformed*** PC12 cells at 37 degrees C exhibit the same
biochemical alterations as those induced in PC12 cells treated with nerve
growth factor. Neurite extension at 37 degrees C in v-src-
***transformed*** cells, like NGF-induced differentiation, is
accompanied by an increase in the nerve growth factor-inducible large
external (NILE) protein. However, neurite extension in v-src-
***transformed*** cells is not blocked by the protein kinase inhibitor
K-252a, which completely blocks NGF-induced neurite extension. Likewise,
EGF receptor down-regulation and the development of saxitoxin and tetanus
***toxin*** binding sites are either much reduced or completely absent
in src-differentiated compared with NGF-differentiated PC12 cells.

=> s l4

'AB' IS NOT A VALID FIELD CODE
L12 57 L4

=> d his

(FILE 'HOME' ENTERED AT 09:24:45 ON 21 SEP 2000)
FILE 'MEDLINE' ENTERED AT 09:24:53 ON 21 SEP 2000
L1 80711 S NEURONAL/AB,BI
L2 5827 S L1 AND (TRANSFECT? OR TRANSFORM? OR TRANSDUC?)/AB,BI
L3 180 S L2 AND TOXIN#/AB,BI
L4 18 S L3 AND VIVO/AB,BI
L5 9 S L3 AND ONCOGENE/AB,BI
L6 2 S L5 AND VIVO/AB,BI
L7 0 S L3 AND TUMORIGENIC AND VIVO/AB,BI
L8 0 S L3 AND TUMORIGENIC/AB,BI
L9 2 S L3 AND IMMORTALIZ?/AB,BI

FILE 'MEDLINE, EMBASE, BIOSIS, INPADOC, CAPLUS' ENTERED AT 09:29:23 ON 21
SEP 2000
L10 19 S L5 OR L6 OR L7 OR L8 OR L9
L11 12 DUP REM L10 (7 DUPLICATES REMOVED)
L12 57 S L4

=> s l12 and transgen?/ab,bi

'AB' IS NOT A VALID FIELD CODE
L13 0 L12 AND TRANSGEN?/AB,BI

=> dup rem l12

PROCESSING COMPLETED FOR L12
L14 25 DUP REM L12 (32 DUPLICATES REMOVED)

=> d 1- bib ab

YOU HAVE REQUESTED DATA FROM 25 ANSWERS - CONTINUE? Y/(N):y

L14 ANSWER 1 OF 25 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.DUPLICATE 1
AN 1999378309 EMBASE
TI Myr+-G(i2).alpha. and G(o).alpha. subunits restore the efficacy of opioids, clonidine and neurotensin giving rise to antinociception in G-protein knock-down mice.
AU Garzon J.; Rodriguez-Diaz M.; DeAntonio I.; DeFelipe J.; Rodriguez J.R.; Sanchez-Blazquez P.
CS J. Garzon, Inst. Neurobiol. Santiago Ramon, Consejo Superior, Investigaciones Cientificas, Avd. Doctor Arce 37, E-28002 Madrid, Spain. jgarzon@cajal.csic.es
SO Neuropharmacology, (1999) 38/12 (1861-1873).
Refs: 47
ISSN: 0028-3908 CODEN: NEPHBW
PUI S 0028-3908(99)00070-2
CY United Kingdom
DT Journal; Article
FS 002 Physiology
022 Human Genetics
029 Clinical Biochemistry

030 Pharmacology
037 Drug Literature Index
008 Neurology and Neurosurgery
LA English
SL English
AB In mice whose Gi/o-protein function had been impaired by antisense 'knock-down' or pertussis ***toxin*** treatment, icv injection of myr+-G(i/o).alpha. subunits restored the effectiveness of .beta.-endorphin, morphine, DPDPE, clonidine and neurotensin to produce antinociception. Myr+-G.alpha. subunits of the class of G-proteins actually impaired were more effective than unlike but related myr+-G.alpha. subunits. Selectivity was noted in that only exogenous myr+-G.alpha. subunits affected (enhanced) the activity of agonists in G.alpha.-deficient signalling systems. This treatment had little effect on agonist potency when the impairment resided at the receptor level. The potential of the opioids, clonidine and R-PIA to increase G.alpha.-related in vitro hydrolysis of GTP was also re-established after injecting myr+-G(i2).alpha. subunits into Gi2-knocked-down mice. Myr+-G(i2).alpha. subunits pre-incubated with GTP.gamma.S or GDP.beta.S before icv injection did not improve the activity of agonists in ***vivo*** (antinociception) or in vitro (regulation of low K(m) GTPase). After impairing the function of PKC.beta.1 by antisense treatment or with the inhibitor H7, the effect of myr+-G.alpha. subunits on agonist potency was prevented. Electron microscope analysis showed the entry of gold-conjugated myr+-G.alpha. subunits into neural cells. These particles were found in the cytoplasm, associated with the plasma membranes of different ***neuronal*** processes and also in synaptic junctions. In cultured neurons and astrocytes myr+-G(i2).alpha.-associated fluorescence was internalised in a dose-dependent manner and distributed in the plasma membrane and cytosol, as well as in nuclei of dividing astrocytes. Thus, G.alpha. subunits in CSF enter into neurons and functionally couple to the receptor-triggered signalling cascade. As G-proteins have been implicated in the pathophysiology of several neural disorders, this finding may be valuable in the therapy of such dysfunctions. Copyright (C) 1999 Elsevier Science Ltd.

L14 ANSWER 2 OF 25 MEDLINE DUPLICATE 2
AN 1999343779 MEDLINE
DN 99343779
TI Chemokine receptor expression and signaling in macaque and human fetal neurons and astrocytes: implications for the neuropathogenesis of AIDS.
AU Klein R S; Williams K C; Alvarez-Hernandez X; Westmoreland S; Force T; Lackner A A; Luster A D
CS AIDS Research Center, Massachusetts General Hospital, Harvard Medical School, Charlestown 02129, USA.. klein.robyn@mgh.harvard.edu
NC AI01519 (NIAID) CA69212 (NCI) AI40618 (NIAID) +
SO JOURNAL OF IMMUNOLOGY, (1999 Aug 1) 163 (3) 1636-46. Journal code: IFB. ISSN: 0022-1767.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 199910
EW 19991002
AB Chemokines are believed to play a role in the neuropathogenesis of AIDS through their recruitment of neurotoxin-secreting, virally infected leukocytes into the CNS. Levels of chemokines are elevated in brains of patients and macaques with HIV/SIV-induced encephalitis. The chemokine receptors CCR3, CCR5, and CXCR4 are found on subpopulations of neurons in the cortex of human and macaque brain. We have developed an in vitro system using both macaque and human fetal neurons and astrocytes to further investigate the roles of these receptors in ***neuronal*** response to inflammation. Here we report the presence of functional HIV/SIV coreceptors CCR3, CCR5, and CXCR4 on fetal human and macaque neurons and CCR5 and CXCR4 on astrocytes immediately ex ***vivo*** and after several weeks in culture. Confocal imaging of immunostained neurons demonstrated different patterns of distribution for these receptors, which may have functional implications. Chemokine receptors were shown to respond to their appropriate chemokine ligands with increases in intracellular calcium that, in the case of neurons, required predepolarization with KCl. These responses were blocked by neutralizing chemokine receptor in mAbs. Pretreatment of neural cells with pertussis ***toxin*** abolished responses to stromal-derived factor-1alpha, macrophage inflammatory protein-1beta, and RANTES, indicating coupling of CCR5 and CXCR4 to a Gialpha protein, as in leukocytes. Cultured macaque neurons demonstrated calcium flux response to treatment with recombinant SIVmac239 envelope protein, suggesting a mechanism by which viral envelope could affect ***neuronal*** function in SIV infection. The presence of functional chemokine receptors on neurons and astrocytes suggests that chemokines could serve to link inflammatory and ***neuronal*** responses.

L14 ANSWER 3 OF 25 MEDLINE DUPLICATE 3
AN 1999192822 MEDLINE
DN 99192822
TI Non-viral ***neuronal*** gene delivery mediated by the HC fragment of tetanus ***toxin*** .
AU Knight A; Carvajal J; Schneider H; Coutelle C; Chamberlain S; Fairweather N
CS Section of Molecular Genetics, ICSM, London, UK.. am.knight@ic.ac.uk
SO EUROPEAN JOURNAL OF BIOCHEMISTRY, (1999 Feb) 259 (3) 762-9. Journal code: EMZ. ISSN: 0014-2956.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199906
EW 19990604
AB Many inherited neurological diseases and cancers could potentially benefit from efficient targeted gene delivery to neurons of the central nervous system. The nontoxic fragment C (HC) of tetanus ***toxin*** retains the specific nerve cell binding and transport properties of tetanus holotoxin. The HC fragment has previously been used to promote the uptake of attached proteins such as horseradish peroxidase, beta-galactosidase and superoxide dismutase into ***neuronal*** cells in vitro and in ***vivo*** . We report the use of purified recombinant HC

fragment
produced in yeast and covalently bound to polylysine [poly(K)] to enable
binding of DNA. We demonstrate that when used to ***transfect***
cells, this construct results in nonviral gene delivery and marker gene
expression in vitro in N18 RE 105 cells (a neuroblastoma x glioma
mouse/rat hybrid cell line) and F98 (a glioma cell line).
***Transfection*** was dependent on HC and was ***neuronal*** cell
type specific. HC may prove a useful targeting ligand for future
***neuronal*** gene therapy.

L14 ANSWER 4 OF 25 MEDLINE DUPLICATE 4
AN 1999198837 MEDLINE
DN 99198837
TI Melatonin receptor potentiation of cyclic AMP and the cystic fibrosis
transmembrane conductance regulator ion channel.
AU Nelson C S; Marino J L; Allen C N
CS Center for Research on Occupational and Environmental Toxicology,
Department of Psychiatry, Oregon Health Sciences University, Portland
97201, USA.
NC AG10794 (NIA)
SO JOURNAL OF PINEAL RESEARCH, (1999 Mar) 26 (2) 113-21.
Journal code: JND. ISSN: 0742-3098.
CY Denmark
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199907
EW 19990704
AB We have used the cystic fibrosis transmembrane conductance regulator
(CFTR) Cl- channel as a model system to study the cAMP signal
***transduction*** pathways coupled to the Xenopus melatonin receptor.
During forskolin (Fsk) stimulation, melatonin reduced the amplitude of the
CFTR currents in oocytes injected with in vitro transcribed cRNAs for the
Xenopus melatonin receptor and CFTR. Pertussis ***toxin*** (Ptx)
treatment eliminated melatonin inhibition of Fsk stimulated CFTR currents.
In oocytes injected with cRNA for melatonin receptors, serotonin receptors
(5-HT7), and CFTR Cl- channels, application of melatonin together with
serotonin (5-HT) activated an additional inward current showing
potentiation of adenylyl cyclases by melatonin receptors. Subthreshold
activation of 5-HT7 receptors was sufficient and necessary to permit
activation of CFTR channels by melatonin. Preexposure to melatonin
desensitized the melatonin receptor mediated response. Therefore, based on
this model system, the effects of melatonin in ***vivo*** could be
either positive or negative modulation of other ***neuronal*** inputs,
depending on the mode of adenylyl cyclase stimulation.

L14 ANSWER 5 OF 25 MEDLINE
AN 1999253888 MEDLINE
DN 99253888
TI GDNF: a novel factor with therapeutic potential for neurodegenerative
disorders.
AU Walton K M
CS Department of Neurobiology, Cephalon, Inc., West Chester, PA 19380, USA.
SO MOLECULAR NEUROBIOLOGY, (1999 Feb) 19 (1) 43-59.
Journal code: AH6. ISSN: 0893-7648.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199908
AB The identification of novel factors that promote ***neuronal***
survival could have profound effects on developing new therapeutics for
neurodegenerative disorders. Glial cell line-derived neurotrophic factor
(GDNF) is a novel protein purified and cloned based on its marked ability
to promote dopaminergic ***neuronal*** function. GDNF, now known to be
the first identified member of a family of factors, signals through the
previously known receptor tyrosine kinase, Ret. Unlike most ligands for
receptor tyrosine kinases, GDNF does not bind and activate Ret directly,
but requires the presence of GPI-linked coreceptors. There are several
coreceptors with differing affinities for the GDNF family members. The
profile of coreceptors in a cell may determine which factor preferentially
activates Ret. In ***vivo*** differences in localization of the GDNF
family members, its coreceptors and Ret suggest this ligand/receptor
interaction has extensive and multiple functions in the CNS as well as in
peripheral tissues. GDNF promotes survival of several ***neuronal***
populations both in vitro and in ***vivo*** . Dopaminergic
***neuronal*** survival and function are preserved by GDNF in
***vivo*** when challenged by the ***toxins*** MPTP and
6-hydroxydopamine. Furthermore, GDNF improves the symptoms of
pharmacologically induced Parkinson's disease in monkeys. Several motor
neuron populations isolated in vitro are also rescued by GDNF. In
***vivo*** , GDNF protects these neurons from programmed cell death
associated with development and death induced by ***neuronal***
transection. These experiments suggest that GDNF may provide significant
therapeutic opportunities in several neurodegenerative disorders.

L14 ANSWER 6 OF 25 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.DUPLICATE 5
AN 1998173146 EMBASE
TI ABT-594 [(R)-5-(2-Azetidinylmethoxy)-2-Chloropyridine]: A novel, orally
effective analgesic acting via ***neuronal*** nicotinic acetylcholine
receptors: I. In vitro characterization.
AU Donnelly-Roberts D.L.; Puttfarcken P.S.; Kuntzweiler T.A.; Briggs C.A.;
Anderson D.J.; Campbell J.E.; Piattoni-Kaplan M.; McKenna D.G.; Wasicak
J.T.; Holladay M.W.; William M.; Americ S.P.
CS Dr. D.L. Donnelly-Roberts, NUDR, Building AP10, Dept. 47W, 100 Abbott Park
Rd., Abbott Park, IL 60064-3500, United States
SO Journal of Pharmacology and Experimental Therapeutics, (1998) 285/2
(777-786).
Refs: 45
ISSN: 0022-3565 CODEN: JPETAB
CY United States
DT Journal; Article
FS 008 Neurology and Neurosurgery
024 Anesthesiology
030 Pharmacology
037 Drug Literature Index
LA English
SL English
AB The discovery of (.+-.)-epibatidine, a naturally occurring
***neuronal*** nicotinic acetylcholine receptor (nAChR) agonist with
antinociceptive activity 200-fold more potent than that of morphine, has
renewed interest in the potential role of nAChRs in pain processing.
However, (.+-.)-epibatidine has significant side-effect liabilities
associated with potent activity at the ganglionic and neuromuscular
junction nAChR subtypes which limit its potential as a clinical

entity.
ABT-594 [(R)-5-(2-azetidinylmethoxy)-2- chloropyridine] is a novel, potent
cholinergic nAChR ligand with analgesic properties (see accompanying paper
by Bannon et al., 1998b) that shows preferential selectivity for ***neuronal*** nAChRs and a consequently improved in ***vivo*** side-effect profile compared with (.+-.)-epibatidine. ABT-594 is a potent
inhibitor of the binding of [3H](-)-cytisine to .alpha.4.beta.2 ***neuronal*** nAChRs (K(i) = 37 pM, rat brain; K(i) = 55 pM, ***transfected*** human receptor). At the .alpha.1.beta.1.delta..gamma.
neuromuscular nAChR labeled by [125I].alpha.-bungaro-***toxin*** (.alpha.- Btx), ABT-594 has a K(i) value of 10,000 nM resulting in a
greater than 180,000-fold selectivity of the compound for the ***neuronal*** .alpha.4.beta.2 nAChR. In contrast, (.+-.)-epibatidine
has K(i) values of 70 pM and 2.7 nM at the .alpha.4.beta.2 and .alpha.1.beta.1.gamma..delta. nAChRs, respectively, giving a selectivity
of only 38-fold. The S-enantiomer of ABT-594, A-98593 has activity at the ***neuronal*** .alpha.4.beta.2 nAChR identical with ABT-594 (K(i) =
34-39 pM), which demonstrates a lack of stereospecific binding similar to
that reported previously for (.+-.)- epibatidine. A similar lack of
stereoselectivity is seen at the human .alpha.7 receptor. However, A-98593
is 3-fold more potant at the neuromuscular nAChR (K(i) = 3420 nM) and the
brain .alpha.-Btx-sensitive nAChR (K(i) = 4620 nM) than ABT-594. ABT-594
has week affinity in binding assays for adrenoreceptor subtypes alpha-1B
(K(i) = 890 nU), alpha-2B (K(i) = 597 nU) and alpha-2C (K(i) = 342 nM),
and it has negligible affinity (K(i) > 1000 nM) for approximately 70 other
receptors, enzyme and transporter binding sites. Functionally, ABT-594 is
an agonist. At the ***transfected*** human .alpha.4.beta.2 ***neuronal*** nAChR (K177 cells), with increased 86Rb+ efflux as a
measure of cation efflux, ABT-594 had an EC50 value of 140 nM with an
intrinsic activity (IA) compared with (-)-nicotine of 130%; at the nAChR
subtype expressed in IMR-32 cells (sympathetic ganglion-like), an EC50 of
340 nM (IA = 126%); at the F11 dorsal root ganglion cell line (sensory
ganglion-like), an EC50 of 1220 nM (IA = 71%); and via direct measurement
of ion currents, an EC50 value of 56,000 nM (IA = 83%) at the human
.alpha.7 homooligimeric nAChR produced in oocytes. A-98593 is 2- to 3-fold
more potent and displays approximately 50% greater intrinsic activity than
ABT-594 in all four functional assays. In terms of potency, ABT-594 is 8-
to 64-fold less active than (.+-.)-epibatidine and also has less IA in
these functional assays. ABT-594 (30 .mu.M) inhibits the release of
calcitonin gene-related peptide from C-fibers terminating in the dorsal
horn of the spinal cord, an effect mediated via nAChRs. Pharmacologically,
ABT-594 has an in vitro profile distinct from that of the prototypic
nicotinic analgesic (.+-.)-epibatidine, with the potential for
substantially reduced side-effect liability and, as such, represents a
potentially novel therapeutic approach to pain management.

L14 ANSWER 7 OF 25 MEDLINE
AN 1998082844 MEDLINE
DN 98082844
TI Contributions of N-linked glycosylation to the expression of a functional
alpha7-nicotinic receptor in Xenopus oocytes.
AU Chen D; Dang H; Patrick J W
CS Division of Neuroscience, Baylor College of Medicine, Houston, Texas
77030, USA.
NC NS13546 (NINDS)
DA04077 (NIDA)
SO JOURNAL OF NEUROCHEMISTRY, (1998 Jan) 70 (1) 349-57.
Journal code: JAV. ISSN: 0022-3042.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199804
EW 19980401
AB The alpha7 subunit of the ***neuronal*** nicotinic acetylcholine
receptor, when expressed in Xenopus oocytes, forms homooligomeric
ligand-gated ion channels that are blocked by a snake ***toxin*** ,
alpha-bungarotoxin. The amino-terminal extracellular domain of the alpha7
sequence has three consensus sites for asparagine-linked glycosylation
(N46DS, N90MS, and N133AS). In this study, we show that alpha7 expressed
either in ***vivo*** or in vitro is a glycoprotein of 57 kDa. In addition, we demonstrate by site-directed mutagenesis that all three consensus sites are used for glycosylation. To elucidate the role(s) of
asparagine-linked glycosylation in the formation and function of the alpha7 receptor, wild-type and glycosylation-deficient alpha7 subunits
were expressed in COS cells and oocytes. We examined biochemical and
physiological properties of expressed receptors and found that alpha7
glycosylation mutations do not affect homooligomerization and surface
protein expression of the alpha7 receptor but do affect surface expression
of alpha-bungarotoxin binding sites and the function of the receptor. Our
data indicate that asparagine-linked glycosylation is required for the expression of a functional alpha7 receptor in oocytes.

L14 ANSWER 8 OF 25 MEDLINE DUPLICATE 6
AN 1998453369 MEDLINE
DN 98453369
TI Landmarks in the application of 13C-magnetic resonance spectroscopy to
studies of ***neuronal*** /glial relationships.
AU Bachelard H
CS MR Centre, Department of Physics, University of Nottingham, UK..
ppzwkp@ppn1.nott.ac.uk
SO DEVELOPMENTAL NEUROSCIENCE, (1998) 20 (4-5) 277-88. Ref: 70
Journal code: EC5. ISSN: 0378-5866.
CY Switzerland
DT (LECTURES)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199903
EW 19990301
AB The development of the use of carbon isotopes as metabolic tracers is
briefly described. 13C-labelled precursors (13CO2, 13CH4) first became
available in 1940 and were studied in microorganisms, but their use was
limited by very low enrichments and lack of suitable analytical equipment.
More success was achieved with 11C and especially 14C, as these radioactive tracers did not need to be highly enriched. Although the
stable 13C isotope can be used at a low percentage enrichment in mass
spectrometry, its application to magnetic resonance spectroscopy (MRS)
requires very highly enriched precursors, due to its low natural abundance
and low sensitivity. Despite such limitations, however, the great

advantage of 13C-MRS lies in its exquisite chemical specificity, in that
labelling of different carbon atoms can be distinguished within the same
molecule. Effective exploitation became feasible in the early 1970s with
the advent of stable instruments, Fourier ***transform*** 13C-MRS, and
the availability of highly enriched precursors. Reports of its use in
brain research began to appear in the mid-1980s. The applications of 13C
isotopomer analysis to research on ***neuronal*** /glial relationships
are reviewed. The presence of neighbouring 13C-labelled atoms affects the
appearance of the resonances (splitting due to C-C coupling), and so
allows for unique quantification of rates through different and possibly
competing pathways. Isotopomer patterns in resonances labelled from a
combination of [1-13C]glucose and [1, 2-13C2]acetate have revealed aspects
of ***neuronal*** /glial metabolic trafficking on depolarization and
under hypoxic conditions in vitro. This approach has now been applied to
in ***vivo*** studies on inhibition of glial metabolism using
fluoroacetate. The results confirm the glial specificity of the
***toxin*** and demonstrate that it does not affect entry of acetate.
When the glial TCA cycle is inhibited, the ability of the glia to
participate in the glutamate/glutamine cycle remains unimpaired, in that
labelling of glutamine, which can only be derived from ***neuronal***
metabolism of glucose, persists. The results also confirmed earlier
evidence that part of the GABA transmitter pool is derived from glial
glutamine.

L14 ANSWER 9 OF 25 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1999:107853 BIOSIS
DN PREV199900107853
TI Congener-specific distribution of polychlorinated biphenyls in brain
regions, blood, liver, and fat of adult rats following repeated exposure
to Aroclor 1254.
AU Kodavanti, Prasada Rao S. (1); Ward, Thomas R. (1); Derr-Yellin, Ethel C.
(1); Mundy, William R. (1); Casey, Ann C.; Bush, Brian; Tilson, Hugh A.
(1)
CS (1) Neurotoxicology Div., National Health Environmental Effects Res. Lab.,
U.S. Environmental Protection Agency, Research Triangle Park, NC 27711 USA
SO Toxicology and Applied Pharmacology, (Dec., 1998) Vol. 153, No. 2, pp.
199-210.
ISSN: 0041-008X.
DT Article
LA English
AB Our previous in vitro studies with both isolated organelles and primary
***neuronal*** cell cultures found that intracellular signal
***transduction*** can be perturbed by some noncoplanar PCBs at exposure
levels of gtoreq 10 muM. However, it is not clear whether such
concentrations are achievable in brain in ***vivo*** . Also, the
pattern of congener disposition and quantities of the PCB accumulation in
tissues of animals exposed to commercial PCB mixtures is not well studied.
In the present study, we have conducted PCB congenerspecific analysis in
different brain regions, liver, blood, and fat of adult male Long-Evans
rats dosed orally with Aroclor 1254 (O or 30 mg/kg/day; once per day, 5
days/week for 4 weeks) in corn oil. Twenty-four hours after the last dose,
rats were euthanized, and the brains were removed and dissected to obtain
cerebellum, frontal cortex, and striatum. Liver, blood, and fat samples
were also collected at the same time. Congener-specific analysis of PCBs
was performed by high-resolution gas chromatography with electron capture
detection. While PCB concentrations in control rat brain regions were less
than 0.02 ppm, total PCB congeners in treated animals accumulated to much
higher levels. Total levels in the frontal cortex, cerebellum, and
striatum were 15.1 +- 0.3, 13.1 +- 1.7, and 8.2 +- 2.6 ppm, respectively.
The levels of PCBs in the fat, liver, and blood were 0.041, 0.002, and
0.001 ppm in control rats and 552, 38.3, and 1.6 ppm in treated rats,
respectively. In addition to the differential total uptake between
tissues, there was differential accumulation of PCBs with respect to the
number of chlorines. In all the tissues, the more lightly chlorinated
(tetra- and penta-) congeners accumulated less than their respective
proportions in the parent Aroclor 1254 mixture. On the other hand, heavily
chlorinated (hexa- to nona-) congeners accumulated more than the
proportion of these congeners found in Aroclor 1254 mixture. This shift
toward accumulation of heavily chlorinated congeners seems to be more
pronounced in the brain than liver and fat. Predominant congeners (5-32%
of total PCBs) detected in different brain regions, blood, liver, and fat
are: 2,3,3',4',5,6- (no. 163) + 2,2',3,4,4',5- (no. 138) (coeluted);
2,2',4,4',5,5'- (no. 153) + 2,2',3,3',4,6'- (no. 132) (coeluted);
2,3,3',4,4',5- (no. 156) + 2,2',3,3',4,4',6- (no. 171) (coeluted);
2,3',4,4',5- (no. 118); 2,2',4,4',5-(no. 99); and 2,3,3',4,4'- (no. 105).
These congeners together accounted for about two thirds of the total PCB
load in brain. AU these predominant congeners are ortho-substituted and
therefore are noncoplanar in nature. The total PCB concentrations
accumulated in brain were as high as 50 IAM (based on average molecular
weight of 326.4 for Aroclor 1254) and, at these concentrations,
intracellular second messengers were significantly affected in
***neuronal*** cultures and brain homogenate preparations in vitro.
These results indicate that concentrations that altered Ca2+ disposition
and second messenger systems in vitro are achievable in brain in
***vivo*** following repeated exposure.

L14 ANSWER 10 OF 25 MEDLINE DUPLICATE 7
AN 1999126974 MEDLINE
DN 99126974
TI Pituitary adenylate cyclase activating peptide (PACAP) in the retinohypothalamic tract: a daytime regulator of the biological clock.
AU Hannibal J; Ding J M; Chen D; Fahrenkrug J; Larsen P J; Gillette M U;
Mikkelsen J D
CS Department of Clinical Biochemistry, Bispebjerg Hospital, University of
Copenhagen, Denmark.. biochbbh@inet.uni2.dk
NC NS22155 (NINDS)
SO ANNALS OF THE NEW YORK ACADEMY OF SCIENCES, (1998 Dec 11) 865 197-206.
Journal code: 5NM. ISSN: 0077-8923.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199904
EW 19990403
AB The retinohypothalamic tract (RHT) relays photic information from the eyes
to the brain biological clock in the suprachiasmatic nucleus (SCN).
Activation of this pathway by light plays a role in adjusting circadian
timing to light exposure at night. Here we report a new signaling pathway
by which the RHT regulates circadian timing in the daytime as well. Using
dual-immunocytochemistry for PACAP and the in ***vivo*** tracer

Cholera ***toxin*** subunit B (ChB), intense PACAP immunoreactivity (PACAP-IR) was observed in retinal afferents at the rat SCN as well as in the intergeniculate leaflet (IGL) of the thalamus. This PACAP-IR was nearly lost upon bilateral eye enucleation. PACAP afferents originated from ganglion cells distributed throughout the retina. The phase of circadian rhythm measured as SCN ***neuronal*** activity in vitro was significantly advanced by application of PACAP-38 during the subjective day, but not at night. The effect is channelled to the clock via a PACAP 1 receptor-cAMP signaling mechanism. Thus, in addition to its role in nocturnal regulation by glutamatergic neurotransmission, the RHT can adjust the biological clock by a PACAP-cAMP-dependent mechanism during the daytime.

L14 ANSWER 11 OF 25 MEDLINE DUPLICATE 8
AN 1999066984 MEDLINE
DN 99066984
TI LIF (AM424), a promising growth factor for the treatment of ALS.
AU Kurek J B; Radford A J; Crump D E; Bower J J; Feeney S J; Austin L; Byrne E
CS AMRAD Corporation Ltd, Melbourne, Australia.. jkurek@amrad.com.au
SO JOURNAL OF THE NEUROLOGICAL SCIENCES, (1998 Oct) 160 Suppl 1 S106-13.
Ref: 64
Journal code: JBJ. ISSN: 0022-510X.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199905
EW 19990503
AB Growth factors are theoretically promising agents for ALS therapy, but have been disappointing in subcutaneous delivery due to either toxicity or lack of major efficacy. Leukaemia inhibitory factor (LIF), was named after its effect on haemopoietic cells, and belongs to a group of cytokines which includes CNTF, IL-6, CT-1, OM and IL-11. All group members use the gp130 signal ***transducing*** subunit for intracellular signalling, but show differences in biological effect. In vitro and in ***vivo*** studies on axotomy and nerve crush models demonstrate a powerful effect of LIF in the survival of both motor and sensory neurones, while reducing denervation induced muscle atrophy. Its effects in muscle also include stimulating myoblast proliferation in vitro, and up-regulation after muscle injury. LIF will also stimulate muscle regeneration in ***vivo*** when applied exogenously after injury. In published studies of both axotomy induced ***neuronal*** death and in the Wobbler mouse models LIF is active at doses of 10 microg/kg delivered systemically, well below the expected maximum tolerated dose suggested by primate safety studies. LIF is expressed in low levels by spinal cord neurones with significant up-regulation when the neurones are damaged by BOAA ***toxin*** , an excitatory amino acid associated with a form of ALS. This augments other evidence suggesting LIF is a trauma factor playing a role in the injury response of adult ***neuronal*** tissue, and may be more effective than related growth factors. Taken together, the data suggests LIF is a physiologically relevant trophic factor with implications in clinical medicine as a therapy for ALS, and a human recombinant form (AM424), entered human clinical trials during 1998.

L14 ANSWER 12 OF 25 CAPLUS COPYRIGHT 2000 ACS
AN 1998:299013 CAPLUS
DN 129:39125
TI Calcium mobilization and protease-activated receptor cleavage after thrombin stimulation in motor neurons
AU Smirnova, Irina V.; Vamos, Suzanne; Wiegmann, Thomas; Citron, Bruce A.; Arnold, Paul M.; Festoff, Barry W.
CS Neurobiology Research, Department of Veterans Affairs Medical Center, Kansas City, MO, 64128, USA
SO J. Mol. Neurosci. (1998), 10(1), 31-44
CODEN: JMNEES; ISSN: 0895-8696
PB Humana Press Inc.
DT Journal
LA English
AB Thrombin, the ultimate enzyme in the blood coagulation cascade, has prominent actions on various cells, including neurons. As in platelets, thrombin increases [Ca2+]i mobilization in neurons, and also retracts neurites. Both these effects are mediated through a G protein-coupled, proteolytically activated receptor for thrombin (PAR-1). Prolonged exposure to thrombin kills neurons via apoptosis that may also involve PAR-1 activation. Increased [Ca2+]i has been a unifying mechanism proposed for cell death in several neurodegenerative diseases. Thrombin-elevated calcium levels may activate intracellular cascades in neurons leading to cell death. Since thrombin mediates its diverse effects on cells through both heterotrimeric and monomeric G proteins, we also explored what effect altering differential G protein coupling would have on the ***neuronal*** response to thrombin. We studied calcium mobilization by thrombin in a model motor ***neuronal*** cell line, NSC19, using fluorescence image anal. Confirming effects in other ***neuronal*** types, thrombin caused dramatic increases in [Ca2+]i levels, both transiently and after prolonged exposure, which involved activation and cleavage of the PAR-1 receptor. Using an enzyme linked immunosorbent assay (ESISA) and dot-blot anal., we found that the N-terminal fragment of PAR-1 was released into the medium after exposure to thrombin. We confirmed that PAR-1 protein and mRNA expression occurred in motor neurons. We found that cholera ***toxin*** inhibited thrombin-mediated Ca2+ influx, pertussis ***toxin*** did not significantly alter thrombin action, and lovastatin, a small 21-kDa Ras GTpase (Rho) modulator, showed a tendency to reduce the thrombin effect. These data indicate that thrombin-increased [Ca2+]i, sufficient to trigger cell death in motor neurons, might by approached in ***vivo*** by modulating thrombin signaling through PAR-1.

L14 ANSWER 13 OF 25 MEDLINE DUPLICATE 9
AN 97218291 MEDLINE
DN 97218291
TI Pituitary adenylate cyclase-activating peptide (PACAP) in the retinohypothalamic tract: a potential daytime regulator of the biological clock.
AU Hannibal J; Ding J M; Chen D; Fahrenkrug J; Larsen P J; Gillette M U; Mikkelsen J D
CS Department of Clinical Biochemistry, Bispebjerg Hospital, University of

Copenhagen, DK-2400 Copenhagen NV, Denmark.
NC NS22155 (NINDS)
SO JOURNAL OF NEUROSCIENCE, (1997 Apr 1) 17 (7) 2637-44.
Journal code: JDF. ISSN: 0270-6474.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199904
EW 19990404
AB The retinohypothalamic tract (RHT) relays photic information from the eyes to the suprachiasmatic nucleus (SCN). Activation of this pathway by light plays a role in adjusting circadian timing via a glutamatergic pathway at night. Here we report a new signaling pathway by which the RHT may regulate circadian timing in the daytime as well. We used dual immunocytochemistry for pituitary adenylate cyclase-activating peptide (PACAP) and the in ***vivo*** tracer cholera ***toxin*** subunit B and observed intense PACAP-immunoreactivity (PACAP-IR) in retinal afferents in the rat SCN as well as in the intergeniculate leaflet (IGL) of the thalamus. This PACAP-IR in the SCN as well as in the IGL was nearly lost after bilateral eye enucleation. PACAP afferents originated from small ganglion cells distributed throughout the retina. The phase of circadian rhythm measured as SCN ***neuronal*** activity in vitro was significantly advanced (3.5 +/- 0.4 hr) by application of 1 x 10(-6) M PACAP-38 during the subjective day [circadian time (CT)-6] but not at night (CT14 and CT19). The phase-shifting effect is channeled to the clock via a PACAP-R1 receptor, because mRNA from this receptor was demonstrated in the ventral SCN by in situ hybridization. Furthermore, vasoactive intestinal peptide was nearly 1000-fold less potent in stimulating a phase advance at CT6. The signaling mechanism was through a cAMP-dependent pathway, which could be blocked by a specific cAMP antagonist, Rp-cAMPS. Thus, in addition to its role in nocturnal regulation by glutamatergic neurotransmission, the RHT may adjust the biological clock by a PACAP/cAMP-dependent mechanism during the daytime.

L14 ANSWER 14 OF 25 MEDLINE DUPLICATE 10
AN 97360054 MEDLINE
DN 97360054
TI Neurotoxicity of soluble macrophage products in vitro--influence of dexamethasone.
AU Flavin M P; Ho L T; Coughlin K
CS Department of Pediatrics, Queen's University, Kingston, Ontario, Canada.
SO EXPERIMENTAL NEUROLOGY, (1997 Jun) 145 (2 Pt 1) 462-70.
Journal code: EQF. ISSN: 0014-4886.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199710
EW 19971001
AB When macrophage conditioned medium is added to neurons in vitro, there is a loss of cell membrane integrity, a loss of cell processes, and a large increase in apoptotic neurons. We tested the influence of a potent anti-inflammatory steroid on the interaction between macrophages and neurons. Dexamethasone was applied to macrophages in culture for 24 h while the culture was stimulated with lipopolysaccharide and hypoxia. Conditioned medium was collected after dexamethasone was removed. The dexamethasone pretreated medium was not toxic to hippocampal neurons in contrast to medium from stimulated macrophages not treated with steroid. The dexamethasone effect was concentration dependent. Pretreatment of macrophages with indomethacin and ***transforming*** growth factor beta had similar but less impressive effects when compared to dexamethasone. The effect of dexamethasone may have been mediated by inhibiting the synthesis or release of neurotoxic macrophage protein(s), as a combination of medium from steroid pretreated macrophages with medium from nontreated macrophages was not neuroprotective. The ***toxin*** (s) did not appear to be tumor necrosis factor alpha or arginase. A role for most neutral proteases was also excluded. We also assessed the consequence of stressing neurons with a mild hypoxic exposure immediately prior to conditioned medium application. Medium from dexamethasone-treated macrophages did not exaggerate hypoxic ***neuronal*** injury, unlike medium from non-dexamethasone-treated macrophages. It did not, however, block the exaggerating effect when coapplied in equal volume with medium from nontreated macrophages. Dexamethasone at 100 nM had no impact when applied directly to neurons while they were being exposed to conditioned medium. This in vitro protection by dexamethasone may be relevant to the demonstrated benefit of glucocorticoids in selected brain and spinal cord conditions. Suspicion of a potential link between this in vitro finding and in ***vivo*** CNS injury justifies an assessment of more specific agents acting on macrophage protein synthesis or secretion.

L14 ANSWER 15 OF 25 MEDLINE DUPLICATE 11
AN 96375823 MEDLINE
DN 96375823
TI Vasoactive intestinal polypeptide modulation of nicotinic ACh receptor channels in rat intracardiac neurones.
AU Cuevas J; Adams D J
CS Department of Molecular and Cellular Pharmacology, University of Miami, School of Medicine, FL 33101, USA.
NC HL-35422 (NHLBI)
HL-07188 (NHLBI)
SO JOURNAL OF PHYSIOLOGY, (1996 Jun 1) 493 ( Pt 2) 503-15.
Journal code: JQV. ISSN: 0022-3751.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199705
AB 1. The effects of vasoactive intestinal polypeptide (VIP) on isolated parasympathetic neurones of rat intracardiac ganglia were examined under voltage clamp using dialysed and perforated patch whole-cell and excised outside-out membrane patch recording configurations. 2. VIP reversibly potentiated nicotinic ACh-evoked whole-cell currents, with half-maximal potentiation (EC50) obtained with 260 pM VIP. However, VIP had no effect on muscarinic ACh-evoked currents, ATP-evoked currents, or depolarization-activated ionic currents in these neurones. 3. VIP-induced potentiation of nicotinic ACh-evoked whole-cell currents was observed following cell dialysis, and was inhibited reversibly by bath application

of the VIP receptor-binding inhibitor L-8-K (5 microM) or the ***neuronal*** nicotinic receptor antagonist mecamylamine (3 microM). 4. The signal ***transduction*** pathway mediating VIP-induced potentiation of nicotinic ACh-evoked currents involves a guanine nucleotide-binding protein (G-protein) but not cyclic AMP. Intracellular application of 100 microM GDP-beta-S, or pre-incubation of neurones with pertussis ***toxin*** , inhibited VIP-induced potentiation of ACh-evoked whole-cell currents. 5. In outside-out membrane patches, co-application of ACh (4 microM) and VIP (4 nM) decreased the duration of closings between bursts and clusters of bursts of ACh single-channel activity relative to control (4 microM, ACh alone). VIP, however, did not alter single ACh receptor channel current amplitude, duration of closings and openings within a burst, or mean burst duration. 6. VIP-induced modification of nicotinic ACh receptor channel kinetics results in an increase in the open-channel probability which is sufficient to account for the VIP-mediated potentiation of nicotinic ACh-evoked whole-cell currents. 7. The potentiation of nicotinic ACh-evoked currents by VIP is likely to account for the altered ***neuronal*** activity observed in the mammalian intracardiac ganglia in ***vivo*** and consequent changes in heart rate and cardiac contractility.

L14 ANSWER 16 OF 25 MEDLINE DUPLICATE 12
AN 97157369 MEDLINE
DN 97157369
TI Calcium in suramin-induced rat sensory neuron toxicity in vitro.
AU Sun X; Windebank A J
CS Department of Neurology, Mayo Clinic and Mayo Foundation, Rochester, MN 55905, USA.
NC NS29769 (NINDS)
SO BRAIN RESEARCH, (1996 Dec 2) 742 (1-2) 149-56.
Journal code: B5L. ISSN: 0006-8993.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199706
EW 19970604
AB Suramin is an experimental chemotherapeutic agent and a neurotoxin which causes a dose-dependent peripheral neuropathy in ***vivo*** and inhibits dorsal root ganglion (DRG) neurite outgrowth in vitro. The mechanism of suramin-induced cyto- and neurotoxicity remains unclear. Calcium is a key signal ***transducer*** in cellular responses to a variety of physiological and pathogenic stimuli. In the present study, we have determined the role of calcium in suramin-induced neurotoxicity in dorsal root ganglion neurons in vitro. Suramin-induced inhibition of neurite outgrowth and induction of ***neuronal*** cell death were dose-related phenomena. A low level of extracellular calcium significantly reduced suramin-induced inhibition of neurite outgrowth and delayed ***neuronal*** cell death in vitro. Nimodipine (100 microM), an L-type voltage-sensitive calcium channel (VSCC) inhibitor, mimicked low calcium medium and protected neurite outgrowth in regular calcium medium supplemented with 300 microM suramin. TMB-8 (100 microM), an inhibitor of intracellular calcium release, failed to protect neurite outgrowth against the ***toxin*** . Calmidazolium (10 microM), a potent calmodulin inhibitor, and calpain inhibitor peptide (CIP, 10 microM) protected neurite outgrowth against suramin. The results support the hypothesis that the calcium signaling system is important in suramin-induced neurotoxicity. Influx of extracellular calcium is more important than release of intracellular calcium in causing cell injury in vitro.

L14 ANSWER 17 OF 25 MEDLINE DUPLICATE 13
AN 95344784 MEDLINE
DN 95344784
TI Pertussis ***toxin*** specifically inhibits growth cone guidance by a mechanism independent of direct G protein inactivation.
AU Kindt R M; Lander A D
CS Department of Biology, Massachusetts Institute of Technology, Cambridge 02139, USA.
SO NEURON, (1995 Jul) 15 (1) 79-88.
Journal code: AN8. ISSN: 0896-6273.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199511
AB An assay employing patterned laminin substrata was used to screen for compounds that disrupt neurite guidance. One molecule, pertussis ***toxin*** , caused neurites to wander from patterns that normally guided them, yet had no significant effect on rates of neurite outgrowth. Wandering was greatest on patterns requiring frequent guidance (e.g., laminin stripes with periodic gaps). Surprisingly, the B oligomer of pertussis ***toxin*** , which lacks the subunit that inactivates G proteins, was equipotent at disrupting neurite guidance. Pertussis ***toxin*** probably acts by binding cell surface carbohydrates, since neurites lacking complex-type N-linked oligosaccharides were insensitive to the effects of the ***toxin*** . The B oligomer also blocked growth cone collapse induced by a brain membrane-derived factor, such factors are thought to act as repulsive guidance cues in ***vivo*** . That a single reagent can inhibit ***neuronal*** responses to both attractive and repulsive guidance cues suggests that such cues may share signaling pathways.

L14 ANSWER 18 OF 25 CAPLUS COPYRIGHT 2000 ACS
AN 1995:951675 CAPLUS
DN 124:1847
TI ***Toxin*** -mediated transfer and expression of genes in nerve cells
AU Mueller, G. P.
CS Sch. of Medicine, Uniformed Services Univ. of the Health Sciences, Bethesda, MD, USA
SO Report (1994), ARO-27890.1-LS; Order No. AD-A290 501, 17 pp. Avail.: NTIS
From: Gov. Rep. Announce. Index (U. S.) 1995, 95(19), Abstr. No. 19-02,072
DT Report
LA English
AB Receptor-Mediated Gene Transfer In the CNS: A Feasibility Study. This research sought to det. the feasibility of using receptor-mediated gene transfer as a mechanism for introducing the expression of foreign genes in nerve cells. DNA carrier systems were constructed using ***neuronal*** ligands that are rapidly internalized by receptor-mediated endocytosis. These proteins, principally wheat germ agglutinin and tetanus ***toxin*** C-fragment, were complexed with high expression reporter genes and applied to nerve cells in vitro, and administered in ***vivo*** into rats. Uptake and expression of the reporter genes were analyzed by std. enzymic and histochem. procedures. While we have

demonstrated, for the first time, that cells in brain can internalize and express plasmid DNA, there is no evidence that this process can be made specific through the introduction of a receptor-mediated mechanism. The findings indicate that; (1) receptor-mediated uptake and expression does occur in the CNS, and (2) lysosomal degrdn. is probably not the underlying basis for our inability to observe expression. From this it may be concluded that receptor-mediated uptake is not an efficient means for directing the expression of foreign genes in nerve cells in ***vivo***

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L14 ANSWER 19 OF 25 MEDLINE
AN 95179327 MEDLINE
DN 95179327
TI Fast inhibition of inwardly rectifying K+ channels by multiple neurotransmitter receptors in oligodendroglia.
AU Karschin A; Wischmeyer E; Davidson N; Lester H A
CS Max-Planck-Institute for Biophysical Chemistry, Gottingen, Germany.
NC GM-29836 (NIGMS)
SO EUROPEAN JOURNAL OF NEUROSCIENCE, (1994 Nov 1) 6 (11) 1756-64.
Journal code: BYG. ISSN: 0953-816X.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199506
AB An essential function of myelinating oligodendroglia in the mammalian central nervous system is the regulation of extracellular potassium levels by means of a prominent inwardly rectifying K+ current. Cardiac and ***neuronal*** K+ inward rectifiers are either activated by hyperpolarizing voltages or controlled by neurotransmitters through the action of receptor-activated G proteins. Neuromodulation of inward rectifiers has not previously been considered as a way to regulate oligodendrocyte function. Here we report the expression of serotonin, somatostatin and muscarinic acetylcholine G protein-coupled receptors in rat brain oligodendrocytes. Activation of these receptors leads to pertussis ***toxin*** -sensitive inhibition of inwardly rectifying K+ channels within < 1 s. By contrast, in the heart and in neurons, similar pathways activate an inwardly rectifying conductance. Thus, transmitter-mediated blockade of inward rectifiers appears to be an oligodendrocyte-specific variation of a common motif for convergent signalling pathways. In ***vivo*** , expression of this mechanism, which may be dependent on neuron-glia signalling, may have a regulatory role in K+ homeostasis during neuron activity in the central nervous system.

L14 ANSWER 20 OF 25 MEDLINE DUPLICATE 14
AN 94170397 MEDLINE
DN 94170397
TI Platelet-activating factor: a putative neuromodulator and mediator in the pathophysiology of brain injury.
AU Yue T L; Feuerstein G Z
CS Department of Cardiovascular Pharmacology, SmithKline Beecham Pharmaceuticals, King of Prussia, PA 19406-0939.
SO CRITICAL REVIEWS IN NEUROBIOLOGY, (1994) 8 (1-2) 11-24. Ref: 88
Journal code: CRR. ISSN: 0892-0915.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199406
AB Platelet-activating factor (1-O-hexadecyl-2-acetyl-sn-glycero-3-phosphocholine [PAF]) is a potent lipid autocoid produced by many cell types. PAF is produced by cultured rat cerebellar neurons and human fetal brain cells, and has been extracted from brain tissue. Multiple PAF receptors have been demonstrated in brain tissue. PAF stimulates intracellular Ca2+ mobilization and phosphatidylinositol (PI) metabolism in ***transformed*** ***neuronal*** cell lines via the PAF receptor, to which both pertussis ***toxin*** (PTX)-sensitive and -insensitive G protein appear to couple. PAF has potent actions on cerebral vessels and cerebral metabolism when administered in ***vivo*** . Direct ***neuronal*** effects of PAF, such as inhibition of acetylcholine release, are observed in vitro. Excessive PAF production in pathological states of the nervous system, such as neurotrauma and stroke, has been shown. In multiple studies in rodent and non-rodent models using highly specific and potent PAF antagonists, reversal or prevention of key consequences of brain injury, such as hypoperfusion following ischemia, reperfusion and edema, inflammatory cell accumulation, neurologic/motor deficits, and ***neuronal*** salvage, has been demonstrated. These studies taken together support a role for PAF as an important mediator in the pathophysiology of brain injury.

L14 ANSWER 21 OF 25 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.DUPLICATE 15
AN 93095396 EMBASE
DN 1993095396
TI Nerve growth factor is a potent inducer of proliferation and ***neuronal*** differentiation for adult rat chromaffin cells in vitro.
AU Tischler A.S.; Riseberg J.C.; Hardenbrook M.A.; Cherington V.
CS Department of Pathology, Tufts University School of Medicine, 136 Harrison Avenue,Boston, MA 02111, United States
SO Journal of Neuroscience, (1993) 13/4 (1533-1542).
ISSN: 0270-6474 CODEN: JNRSDS
CY United States
DT Journal; Article
FS 005 General Pathology and Pathological Anatomy
008 Neurology and Neurosurgery
021 Developmental Biology and Teratology
030 Pharmacology
037 Drug Literature Index
LA English
SL English
AB Adult rat chromaffin cells in vitro show a large proliferative response to NGF, followed by ***neuronal*** differentiation. Infection of replicating chromaffin cells with a retrovirus carrying the Escherichia coli .beta.- galactosidase (.beta.-gal) gene demonstrates .beta.-gal expression in cells that continue to multiply, that differentiate into neurons, and that become static. The effects of NGF on proliferation and differentiation are abolished by the protein kinase inhibitors K252a and staurosporine, and by cholera ***toxin*** , an activator of adenylate cyclase. They are diminished, but not abolished, by high concentrations of dexamethasone. Both cholera ***toxin*** alone and phorbol myristate acetate (PMA), an activator of protein kinase C, elicit small and inconsistent mitogenic responses. The responses to PMA cannot be shown to be additive with the effects of NGF. NGF is a known mitogen and neuritogen for chromaffin cells from neonatal rats, but has not previously been believed to affect similarly chromaffin cells from adults. The present findings suggest that portions of NGF signaling pathways might continue to be involved in regulating proliferation of adult rat chromaffin cells in

***vivo*** , and might be constitutively activated in PC12 cells and other adrenal medullary tumors. They further suggest that rat chromaffin cells might be propagated in vitro to obtain large numbers of sympathetic neurons expressing normal or exogenous genes.

L14 ANSWER 22 OF 25 MEDLINE DUPLICATE 16
AN 94037127 MEDLINE
DN 94037127
TI Metabolic mapping with cellular resolution: c-fos vs. 2-deoxyglucose.
AU Sharp F R; Sagar S M; Swanson R A
CS Department of Neurology, University of California at San Francisco..
NC NS27864 (NINDS)
NS27488 (NINDS)
SO CRITICAL REVIEWS IN NEUROBIOLOGY, (1993) 7 (3-4) 205-28. Ref: 159
Journal code: CRR. ISSN: 0892-0915.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LA English
FS Priority Journals
EM 199402
AB 2-Deoxyglucose (2DG) studies have been most useful in mapping activated regions of the nervous system. Cellular localization studies using 2DG have been less rewarding, but results are consistent with current views that increases of 2DG accumulation produced by synaptic activation represent increases in glycolytic glucose metabolism occurring mainly in presynaptic ***neuronal*** and possibly glial elements. Immediate early genes (IEGs), including the fos, jun, and NGFI-A families, are induced by a wide variety of intracellular signaling pathways. The nuclear localization of the protein products of these genes and their induction by a variety of stimuli make them useful in metabolic activation studies carried out at the cellular level. IEGs have been induced in neurons by osmotic, bacterial endotoxin, steroids, stress, and other hormonal stimuli; by light, auditory, painful, and other sensory stimuli; during stimulation of motor cortex and other motor behaviors; and by various drugs and ***toxins*** that act on a variety of neurotransmitter systems, including dopamine and glutamate. In addition, the localization of c-fos gene expression identifies cells that respond to growth factors in ***vivo*** . Retinal Muller cells, the major glial cell type of the retina, demonstrate nuclear Fos immunostaining after the intravitreal injection of epidermal growth factor (EGF) or ***transforming*** growth factor-alpha (TGF-alpha). This observation demonstrates that adult glia can respond to these growth factors in ***vivo*** . The investigation of early response gene expression may be particularly useful for elucidating the role of trophic factors in the cellular response to central nervous system injury.

L14 ANSWER 23 OF 25 MEDLINE
AN 94191900 MEDLINE
DN 94191900
TI In vitro labeling strategies for identifying primary neural tissue and a ***neuronal*** cell line after transplantation in the CNS.
AU Onifer S M; White L A; Whittemore S R; Holets V R
CS Department of Cell Biology and Anatomy, University of Miami School of Medicine, FL 33136.
NC NS26887 (NINDS)
NS07044-16 (NINDS)
SO CELL TRANSPLANTATION, (1993 Mar-Apr) 2 (2) 131-49.
Journal code: B02. ISSN: 0963-6897.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199407
AB Potential labels for identifying embryonic raphe neurons and a clonal, neuronally differentiating, raphe-derived cell line, RN33B, in CNS transplantation studies were tested by first characterizing the labels in vitro. The labels that were tested included 4',6-diamidino-2-phenylindole hydrochloride, 1,1'-dioctadecyl-3,3,3'-tetramethylindocarbocyanine perchlorate, the Escherichia coli lacZ gene, Fast Blue, Fluoro-Gold, fluorescein-conjugated latex microspheres, fluorescein isothiocyanate-conjugated or nonconjugated Phaseolus vulgaris leucoagglutinin, methyl o-(6-amino-3'-imino-3H-xanthen-9-yl) benzoate monohydrochloride, or tetanus ***toxin*** C fragment. Subsequently, the optimal in vitro labels for embryonic raphe neurons and for RN33B cells were characterized in ***vivo*** after CNS transplantation. In vitro, 1,1'-dioctadecyl-3,3,3'-tetramethylindocarbocyanine perchlorate (DiI) optimally labeled embryonic neurons. The Escherichia coli lacZ gene optimally labeled RN33B cells. Most labels were rapidly diluted in cultures of embryonic astrocytes and proliferating RN33B cells. Some labels were toxic and were often retained in cellular debris. In ***vivo*** , DiI was visualized in transplanted, DiI-labeled raphe neurons, but not in astrocytes up to 1 mo posttransplant. DiI-labeled host cells were seen after transplantation of lysed, DiI-labeled cells. beta-Galactosidase was visualized in transplanted, Escherichia coli lacZ gene-labeled RN33B cells after 15 days in ***vivo*** . No beta-galactosidase was seen in host cells after transplantation of lysed, lacZ-labeled RN33B cells. The results demonstrate that labels for use in CNS transplantation studies should be optimized for the specific population of donor cells under study, with the initial step being characterization in vitro followed by in ***vivo*** analysis. Appropriate controls for false-positive labeling of host cells should always be assessed.

L14 ANSWER 24 OF 25 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 17
AN 1992:502612 BIOSIS
DN BA94:121137
TI CILIA FROM ABALONE LARVAE CONTAIN A RECEPTOR-DEPENDENT G PROTEIN ***TRANSDUCTION*** SYSTEM SIMILAR TO THAT IN MAMMALS.
AU BAXTER G T; MORSE D E
CS MARINE BIOTECHNOL. CENT., UNIV. OF CALIFORNIA, SANTA BARBARA, CALIFORNIA 93106.
SO BIOL BULL (WOODS HOLE), (1992) 183 (1), 147-154.
CODEN: BIBUBX. ISSN: 0006-3185.
FS BA; OLD
LA English
AB Lysine and related diamino acids amplify (facilitate) the response to inducers of metamorphosis in larvae of the marine mollusk Haliotis rufescens. Previous studies showed that a cholera ***toxin*** -sensitive G protein ***transduces*** the lysine signal via a diacylglycerol-dependent pathway. We have isolated and partially purified larval cilia that may be involved in recognizing the facilitating chemical signals. These isolated cilia provide an open or porous membrane-associated sensory system that is uniquely tractable for in vitro analyses of chemosensory signal ***transduction*** . The cilia contain receptors that exhibit sodium-independent binding of the facilitating diamino acids. The binding strength for lysine and related diamino acids in vitro is correlated with the effectiveness of these

ligands as facilitators in ***vivo*** . The cilia contain a cholera ***toxin*** -sensitive G protein functionally coupled to the lysine receptor. The receptor and the G protein reciprocally regulate one another, suggesting that the chemosensor may be a member of the rhodopsin-like, G-protein-coupled transmembrane receptor superfamily. Previous analyses of mRNAs from the larval cilia revealed a sequence coding for a G protein with high homology to Gq from mammalian brain, and another sequence coding for a protein homologous to Gi/Go. Similarities between this system, other chemosensory signal ***transduction*** pathways, and mechanisms of ***neuronal*** long-term potentiation are evident. Because the receptors and ***transducers*** controlling settlement and metamorphosis in Haliotis and other marine invertebrate larvae appear homologous to components controlling ***neuronal*** activity, cellular proliferation, and differentiation in mammals, characterization of the molecules controlling metamorphosis may help in the design of new regulators useful in medicine.

L14 ANSWER 25 OF 25 MEDLINE
AN 92343492 MEDLINE
DN 92343492
TI NMDA receptor-mediated arachidonic acid release in neurons: role in signal ***transduction*** and pathological aspects.
AU Lazarewicz J W; Salinska E; Wroblewski J T
CS Fidia-Georgetown Institute for the Neurosciences, Georgetown University School of Medicine, Washington DC.
SO ADVANCES IN EXPERIMENTAL MEDICINE AND BIOLOGY, (1992) 318 73-89.
Journal code: 2LU. ISSN: 0065-2598.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199210
AB The N-methyl-D-aspartate (NMDA)-sensitive subtype of glutamate receptor, which gates Ca(2+)-permeable ion channels, is known for its role in learning and memory formation, in the induction of long-term potentiation, and also in seizure activity and neurotoxicity. In primary cultures of cerebellar neurons, agonists of NMDA receptors induce a dose-dependent release of [3H]arachidonic acid ([3H]AA), which is potentiated by activation of the glycine-positive modulatory site and inhibited by NMDA receptor antagonists. NMDA receptor-induced [3H]AA release is inhibited by quinacrine and partially depends on the presence of extracellular calcium. The [3H]AA release is not sensitive, however, to pretreatment with pertussis or cholera ***toxin*** , which suggests a Ca(2+)-dependent activation of phospholipase A2 not employing G proteins. Pretreatment of cultures with the natural and semisynthetic sphingolipids GT1b and PKS 3, respectively, inhibits NMDA receptor-mediated [3H]AA release. We also demonstrated glutamate-evoked [3H]AA release from rat hippocampal slices, which is NMDA receptor mediated, calcium dependent and sensitive to quinacrine. Arachidonic acid and its metabolites have been shown to play a role as second messengers and to modulate ***neuronal*** activity. Moreover, they are thought to act as transsynaptic modulators in the mechanism of NMDA receptor-induced long-term potentiation in the hippocampus. Their role in ischemic brain pathology has also been postulated. Our experiments on cultured cerebellar granule cells, incubated in a Mg(2+)-free medium deprived of glucose and oxygen, demonstrated a time-dependent stimulation of [3H]AA release. This release was inhibited by antagonists of NMDA receptors and by quinacrine. Stimulation of NMDA-sensitive glutamate receptors and the subsequent calcium-mediated activation of phospholipase A2 may play a role in the in ***vivo*** release of arachidonic acid during brain ischemia. This hypothesis is supported by the observation that the enhanced level of thromboxane B2 in the gerbil brain after 5 min of global ischemia is reduced by the systemic application of either the NMDA antagonist MK-801 or the ganglioside GM1.

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FILE 'MEDLINE' ENTERED AT 09:24:53 ON 21 SEP 2000
L1 80711 S NEURONAL/AB,BI
L2 5827 S L1 AND (TRANSFECT? OR TRANSFORM? OR TRANSDUC?)/AB,BI
L3 180 S L2 AND TOXIN#/AB,BI
L4 18 S L3 AND VIVO/AB,BI
L5 9 S L3 AND ONCOGENE/AB,BI
L6 2 S L5 AND VIVO/AB,BI
L7 0 S L3 AND TUMORIGENIC AND VIVO/AB,BI
L8 0 S L3 AND TUMORIGENIC/AB,BI
L9 2 S L3 AND IMMORTALIZ?/AB,BI

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L10 19 S L5 OR L6 OR L7 OR L8 OR L9
L11 12 DUP REM L10 (7 DUPLICATES REMOVED)
L12 57 S L4
L13 0 S L12 AND TRANSGEN?/AB,BI
L14 25 DUP REM L12 (32 DUPLICATES REMOVED)

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